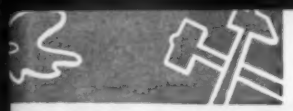

SCIENCE

OCTOBER 10, 1952

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Contents

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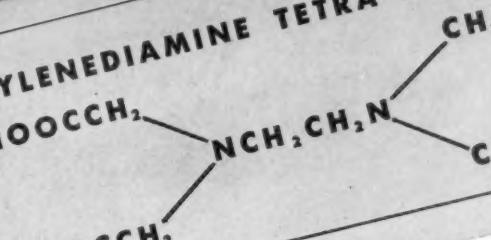

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British Manpower

SEVERAL governmental and professional agencies are concerned with a continuing supply of scientists and technologists to meet this country's expanding needs in defense and industry. These agencies, however, have failed to impress the Congress and the public with the magnitude and urgency of the problem, and comparatively few students of the subject emphasize sufficiently the imperative need for expert teachers in the several fields of science and technology. Comparable situations confront the other industrial nations, and the acute concern that is developing in the United Kingdom with regard to manpower has recently been set forth in the *Fifth Annual Report of the Advisory Council on Scientific Policy (1951–1952)*, from which the following excerpts have been taken.

The Committee on Scientific Man-Power was appointed by the Advisory Council on Scientific Policy in December, 1950. Our terms of reference are "to study the future needs of scientific and technological man-power for employment both at home and abroad." . . . We cannot pay our way in the world or discharge our obligations unless there is a large increase in national production. . . . This must be accomplished with a labor force that is aging fast and which is relatively stable in numbers. . . . The number of young persons reaching the age of 15 was 740,000 in 1939 and 635,000 in the present year. There will be little improvement until 1960. . . . The implications are unmistakable. Manpower must be used with the greatest efficiency. . . . We need to increase both absolutely and relatively the number of scientists in our industries. . . . In 1949–50 the number of American university degrees awarded in science and technology was 110,000, whereas in Great Britain the total . . . was only 14,000. Even when we allow for the difference in the size of the labor force in the two countries, America is thus turning out, and presumably employing, nearly three times as many scientists as we are in Great Britain. . . .

The current demand for scientists arising from industry, the defense program, government service, and plans for assisting the undeveloped areas of the world is so great that we can see no prospect of supply exceeding demand. . . . There is likely to be a long-term shortage of practically all kinds of scientists, and every effort should be made to increase the supply, with particular emphasis on chemists, chemical engineers, electrical engineers, mechanical engineers, and physicists. At present the supply of geologists, civil engineers and metallurgists appears to be equal to the demand. There is some unemployment of men trained primarily in the basic biological sciences. . . .

About 7 per cent of pupils remain at school after the age of 17. . . . A large potential reserve of university students is contained in the number who leave school before the age of 17. . . . The ranks of those who are at present attracted to an arts course provide another potential source of science students. The number of students of pure and applied science at British universities has more than doubled since the war. The numbers in medicine have changed little, whereas those in arts have increased. . . . We do not advocate the diminution in the importance of the humanities in our universities, but many arts graduates are finding it difficult to obtain employment. . . . The technical colleges could be geared to increase their output of scientists within a comparatively short time, but what is clearly needed as well is the further expansion of facilities for scientific education in the universities. . . .

Although present-day science graduates are adequate as scientists, they tend to lack a sufficiently broad education, not only in a general sense but also in the field of science. . . . The narrow specialist is rarely able to step outside the confines of his own particular interests. . . . Particular attention needs to be drawn to the difficulty of finding good science masters. . . . It may become necessary to take special measures to increase the numbers of science teachers in the schools. . . . We need to look now to a steady growth in the facilities for training scientists.

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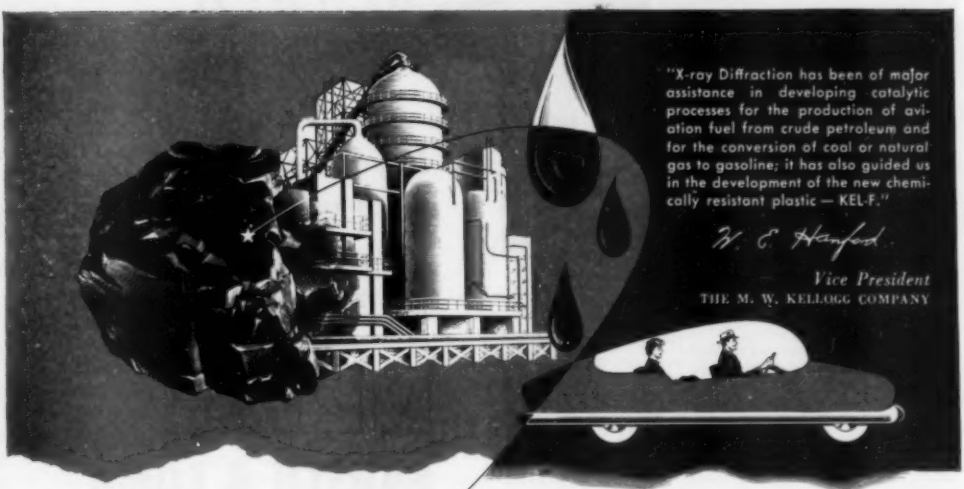

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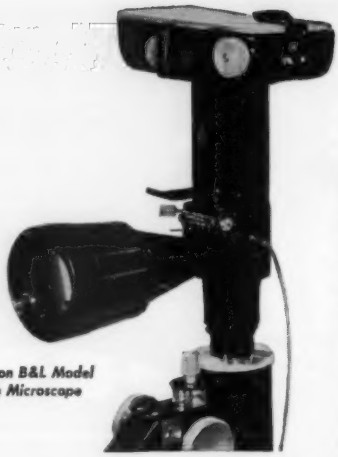

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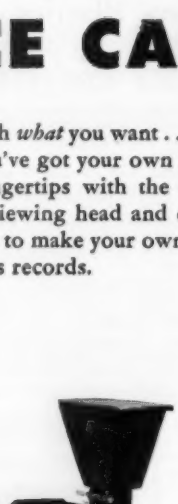

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A New Antifertility Factor[1]

(A Preliminary Report)

Benjamin F. Sieve

The Benjamin F. Sieve, M.D., Clinic, Boston, Massachusetts

SINCE 1949 the author has been working on an orally administered factor that promises safe and controllable antifertility activity. This work was undertaken after Beiler and Martin's (*1*) discovery of a new antihemorrhagic factor which, *in vitro* and *in vivo* in animals, had direct inhibitory action on the enzyme hyaluronidase. They found that the sulfonated and phosphorylated hespiridins inhibited materially the enzymic action of hyaluronidase. Recent reports (*2*) have specifically established a relationship of hyaluronidase to the coronal cells of the ova by a dispersion action. This action is identical with the so-called spreading factor of Duran-Reynals (*3*), which was corroborated later by McClean (*4*).

Hyaluronic acid is a mucopolysaccharide acid found in almost all animal tissues. Myer's (*5*) classic experiments showed that the gels formed by hyaluronic acid are a part of the viscous barriers that regulate the exchange of various metabolites and water. Earlier experiments (*6*) proved that at strategic points in the organism hyaluronic acid gels are disaggregated and depolymerized by the action of the enzyme hyaluronidase. This action reduces the viscosity of this "tissue cement." Myer further demonstrated that the enzyme hyaluronidase acts specifically by hydrolyzing hyaluronic acid.

It was this work that formed the basis for the hypothesis that when the hyaluronidase is in proper concentration in the cells of the spermatozoa and ovum and in the surrounding interstitial fluids, a hesperidin derivative at the proper saturation may act as an inhibitor, and this inhibitory action on the hyaluronidase occurs at the moment when the sperm comes in contact with the coronal cell layer of the ovum. It is now known (*5*) that in the presence of the hesperidin derivative the entire coronal cell layer remains intact, and, in addition, more "tissue cement" is formed, both of which surround the ovum to form an impregnable barrier to the piercing spermatozoa.

The problem of obtaining the most soluble form of hesperidin that could be administered orally or intravenously had been solved by Beiler and Martin (*7*), who showed that phosphate groups may potentiate the action of inhibitors on enzyme systems. Insofar as hyaluronidase itself is an enzyme, it was assumed that phosphorylated hesperidin would be ideal.

Martin (*8*) also proved by animal experimentation that phosphorylated hesperidin[2] was well tolerated and definitely had antifertility action.[2] In his experiments, groups of 20 male and female mice had been given doses of phosphorylated hesperidin intraperitoneally, at a level of 20 mg/kg. After one week of such daily dosage the females were exposed to the males for fertilization, while the same daily dosage was continued in the treated mice. The incidence of fertility was determined by actual deliveries. Normal males were crossed with normal females, resulting in 100 per cent pregnancy. Normal females were crossed with phosphorylated-hesperidin–treated males, with 100 per cent pregnancy. Phosphorylated-hesperidin–treated females were crossed with normal males, resulting in only 11 per cent pregnancy, and phosphorylated-hesperidin–treated females were crossed with phosphorylated-hesperidin–treated males, resulting in 11 per cent pregnancy.

To substantiate and corroborate these figures a series of animal experiments was carried out by the author, of which the following is an example.[3] Twenty male and 20 female healthy white Swiss mice, weighing 25–35 g, were selected for the experiment. The drug was administered in a solution made up from the oral tablet used clinically. Ten female and 10 male mice were given phosphorylated hesperidin in a dosage of 20 mg/kg intraperitoneally, daily for 7 days. On the eighth day, or 24 hours following final injection, mating proceeded as follows:

Group I: Five untreated females with 5 untreated males.
Group II: Four untreated females with 4 phosphorylated-hesperidin–treated males.
Group III: Six phosphorylated-hesperidin–treated females with 6 untreated males.
Group IV: Five phosphorylated-hesperidin–treated females with 5 phosphorylated-hesperidin–treated males.

Table 1 shows the percentage of pregnancies in mice treated with phosphorylated hesperidin. In this group treatment was deliberately omitted after the preliminary 7-day saturation period before mating, in order

[1] Submitted for publication Dec. 18, 1951. Originally this manuscript was prepared as a preliminary report on 50 couples from a series of more than 300. Data were brought up to date in September 1952, to include the entire group of 300 couples. A supplementary report will be published later on the time interval from delivery date to date on which control began, lactation period postpartum to concluding date of lactation, and possible effect of phosphorylated hesperidin on lactation.

[2] Only one known radical of phosphorylated hesperidin, having the correct position on the benzene ring, with a specific pH, has antifertility action. This action cannot be anticipated from just any radical of phosphorylated hesperidin.

[3] The author wishes to acknowledge the cooperation and assistance in these animal experiments, of Howard E. Lind, director, Sias Laboratories, Brooks Hospital, Brookline, Mass.

TABLE 1

PREGNANCIES IN NORMAL AND PHOSPHORYLATED-HESPERIDIN–TREATED MICE

(Medication omitted after 7 days)

	Normal males (%)	Phosphorylated-hesperidin–treated males (%)
Normal females	100	50
Phosphorylated-hesperidin–treated females	67	80

TABLE 2

PREGNANCIES IN NORMAL AND PHOSPHORYLATED-HESPERIDIN–TREATED MICE

(Medication continued through mating period)

	Normal males (%)	Phosphorylated-hesperidin–treated males (%)
Normal females	100	83
Phosphorylated-hesperidin–treated females	60	66

to provide a statistical comparison with the second group, which was treated through the saturation period and continued throughout the mating period.

The second experiment was carried out with a similar number of white mice of the same classification and weight levels. In Group I the controls remained untreated. Groups II, III, and IV were treated identically with those in the first experiment for the first 7 days. On the eighth day the females were exposed to the males for fertilization, but intraperitoneal injections in dosage of 20 mg/kg were continued daily. Table 2 shows the percentage of pregnancies in the second experiment.

Groups of 5 females in both experiments were checked for estrus cycles, which remained unchanged. Microscopic examination of the seminal fluid from males of both groups showed a normal sperm count and normal motility. Subsequent omission of phosphorylated hesperidin showed all females to be again fertile. The males, when taken off treatment and mated with normal healthy female mice, again produced 100 per cent pregnancies.

This animal evidence indicated that no permanent sterility in either sex was to be feared from phosphorylated-hesperidin therapy. This information was important in relation to anticipated work with human beings.

The discrepancies in percentage between Martin's original experiments (*8*) and ours are reconciled in the published report of Martin and Beiler (*9*). Repeated experiments are being carried out on similar groupings of white mice, but with a dose of 40 mg phosphorylated hesperidin per kilogram as the dosage level. In spite of the discrepancy between our results and Martin's, every group treated with phosphorylated hesperidin, including treated males, showed some percentage of fertility control, as compared to 100 per cent pregnancies in the untreated groups.

It can be concluded from the animal experiments that there is definite impairment of fertility of the mice under treatment with phosphorylated hesperidin. On the basis of the studies cited, it is presumed that the impairment is in the inhibition of hyaluronidase. Although the accumulated animal evidence was not as strong as desired, our previous clinical experience with hesperidin was sufficient to warrant studies in human beings.

The author had been using phosphorylated hesperidin in another clinical problem. On the basis of our own clinical experience the drug had been found to be nontoxic both to the organism and to tissues, easily assimilated, and nonaccumulative, and it caused no allergic reactions. These clinical data established the fact that for oral administration the drug could best be dispensed in 100-mg tablets. Therefore this unit of dosage suggested itself as best for the human antifertility experiments.

CLINICAL MATERIAL

This report deals with 300 couples who had been taking the new antifertility factor over varying periods, up to 30 months. The basis for selection of married couples was a history of easy impregnation and normal delivery, with the birth of at least one normal child, thereby, for all practical purposes, ruling out the question of sterility. In two cases, however, a question of sterility following one normal pregnancy and delivery did exist. The reason for including them in the study will be discussed later. Included in the group were individuals with infections, systemic diseases, traumatic injuries, and varying pathologies.

Variations in age groups represented five periods in the reproductive years. Control periods were varied for statistical study. Couples were selected not only from the author's own group of patients, but also from other groups not under his care, in order to eliminate any possible influence in the therapy given to his own patients.

No separate control group was employed in this study. The couples participating in the experiment constituted adequate controls in themselves, as shown by the fertility statistics presented in Tables 3–6. Moreover, no one could either ethically or morally ask any human couple to volunteer for a study of fertility control and then deliberately dispense placebos. Couples who had been under the author's therapy had no fear of taking this drug, as many had been taking the hesperidin factor without difficulty for 12–25 months as an antihemorrhagic factor. These couples were not fearful of pregnancy, as they were mentally and financially prepared for another pregnancy. Their faith in the author, from previous treatment, was great enough for them to say, "If you are satisfied with your animal experiments and the safety of the drug, and you know it will not cause permanent sterility, then

TABLE 3

GROUP I—43 COUPLES (14.3%) AGES 17–22 (FEMALE)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
1	17	(22)	1	350	400	6	7.5	(X)	7	12	Continuing Ⅱ
2	19	(24)	1	350	400	3	11	(X)	4.5	13	Continuing Ⅱ (26-day cycle); intravenous toxicity test, 10 consecutive days up to 20 g daily
3	20	(22)	1	350	450	4	8	(X)	4	14	Continuing Ⅱ
4	21	(23)	1	300	300	8	9	(X)	6	7	Omit Ⅱ; ♀ 6 wk 3rd pregnancy (fertility period only 5 wk)
5	21	(26)	2	350	400	4	6	(X)	5	14	Continuing Ⅱ
6	22	(25)	1	350	450	12	13	X(5)	—	—	Patient about 5 mo pregnant
7	22	(27)	2	350	400	16	—	—	—	—	Couple desire no more children; continuing Ⅱ
8	22	(24)	1	300	450	4	7	(X)	6	14	Continuing Ⅱ
51	17	(19)	1	300	350	7	5	X(7)	—	—	Patient about 7 mo pregnant
52	17	(20)	1	450	400	9	10	(X)(C)	8	5	Patient continuing Ⅱ; *C* = cesarean section
53	18	(18)	1	350	350	10	10	X(4)	—	—	Patient about 4 mo pregnant
54	18	(21)	2	350	300	26	—	—	—	—	Couple desire no more children; male has cancer
55	19	(22)	1	300	300	16	7	(X)(P)	6	2	Continuing Ⅱ; *P* = premature delivery at 8 mo
56	19	(19)	1	300	400	11	6	X(6)	—	—	Patient about 6 mo pregnant
57	19	(20)	2	300	400	8	12	(X)	4	4	Continuing Ⅱ
58	19	(18)	1	400	350	28	—	—	—	—	Couple desire no more children; continuing Ⅱ
59	20	(20)	3	350	450	12	8	(X)	5	3	Continuing Ⅱ
60	20	(21)	1	300	350	7	11	(X)(P)	8	5	Continue Ⅱ; premature delivery at 7.5 mo infant normal weight at 3 mo
61	20	(24)	2	350	400	9	5	(X)	6	4	Continuing Ⅱ
62	20	(26)	2	300	350	6	—	—	—	—	Patient not heard from since
63	20	(25)	1	250	300	13	9	X(4)	—	—	Patient about 4 mo pregnant
64	20	(21)	1	350	400	20	7	X(9)	—	—	Patient at 9 mo is overdue 3 wk
65	21	(22)	3	400	400	18	9	X(3)	—	—	Patient about 3 mo pregnant
66	21	(20)	1	300	350	5	8	(X)	7	2	Continuing Ⅱ
67	21	(24)	2	350	450	6	7	(X)	5	3	" "
68	21	(23)	1	300	400	15	8	X(7)	—	—	Patient about 7 mo pregnant
69	21	(26)	2	350	450	21	6	X(2)	—	—	Patient about 2 mo pregnant
70	21	(28)	3	450	300	15	—	—	—	—	Continuing Ⅱ; couple desire no more children; tuberculosis-active
71	21	(22)	1	300	350	7	5	(X)	6	5	Continuing Ⅱ
72	21	(23)	1	300	400	12	11	X(8)	—	—	Patient about 8 mo pregnant; mild diabetic
73	21	(24)	1	250	300	6	7	(X)	6	3	Continuing Ⅱ
74	21	(26)	2	500	400	13	7	X(M-3)	—	—	Patient miscarried at 12 wk; bronchial asthma
75	22	(25)	1	300	350	5	8	(X)	7	2	Continuing Ⅱ
76	22	(23)	3	400	350	11	12	X(7)	—	—	Patient about 7 mo pregnant
77	22	(23)	1	350	400	26	—	—	—	—	Continuing Ⅱ; couple desire no more children; chronic lymphatic leukemia
78	22	(24)	3	400	350	7	5	(X)	4	5	Continuing Ⅱ
79	22	(27)	2	300	350	18	5	X(4)	—	—	Patient about 4 mo pregnant
80	22	(27)	1	350	400	4	6	(X)	6	3	Continuing Ⅱ
81	22	(28)	2	300	350	3	7	(X)	6	4	" "
82	22	(28)	1	350	300	14	10	X(6)	—	—	Patient about 6 mo pregnant
83	22	(29)	3	400	450	5	—	—	—	—	Patient not heard from since
84	22	(30)	1	300	400	8	6	(X)	5	2	Continuing Ⅱ
85	22	(30)	4	300	400	23	—	—	—	—	Continuing Ⅱ; desire no more children

we have the faith in you to go along with the experiment."

As a further assurance, a pledge was obtained from each couple that only this oral method of fertility control would be employed throughout the experiment.

All patients undergoing study were examined for possible pathological findings and nutritional status. A complete history was taken, and physical examination, urine analysis, complete blood counts, and chemistries were done.

TABLE 4

GROUP II—158 COUPLES (52.6%) AGES 23–30 (FEMALE)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
9	23	(39)	2	400	600	4.5	7	(X)	6	13	Continuing B
10	23	(24)	1	400	450	21	8	X(5)	—	—	Patient about 5 mo pregnant; couple toxicity study; intravenous 10 consecutive days up to 20 g daily
11	23	(26)	1	400	450	10	4	(X)	6	8	Continuing B; this patient was a questionable sterility case previous to therapy
12	23	(25)	1	400	500	8	7	(X)	8	9	Continuing B
13	24	(29)	2	400	500	15	8	X(8)	—	—	Patient about 8 mo pregnant; diabetes mellitus
14	24	(26)	1	350	400	8	7	(X)	8	8	Continuing B
15	24	(31)	2	400	500	6	9	(X)	5	10	" "
16	24	(28)	1	300	350	7	8	(X)	6	9	" "
17	24	(24)	1	350	400	8	6	(X)	9	9	" "
18	25	(27)	2	300	450	5	12	(X)	6	10	" "
19	25	(34)	2	350	500	8	8	(X)	5	8	" "
20	25	(30)	1	450	550	3	6	(X)	7	14	Continuing B; this patient was a questionable sterility case previous to therapy
21	25	(26)	1	400	450	8	7	(X)	6	9	Continuing B
22	25	(26)	2	450	600	13	8	X(7)	—	—	Patient about 7 mo pregnant
23	26	(27)	3	300	300	7	7	(X)	8	10	Continuing B
24	26	(32)	1	600	1100	3	8	(X)	6	12	Continuing B; high-dosage B in male to be reported later
25	27	(34)	1	300	300	4	7	(X)	5	14	Continuing B
26	27	(28)	1	300	400	3	4	(X)	4	10	Continuing B; patient at 6 mo of pregnancy had virus infection, diarrhea, and vomiting
27	28	(35)	1	250	300	22	8	X(6)	—	—	Patient about 6 mo pregnant
28	28	(30)	1	350	450	6	4	(X)	6	12	Continuing B
29	28	(28)	2	500	550	29	—	—	—	—	Couple desire no more children; continuing B
30	29	(28)	1	350	450	5	7	(X)	8	11	Continuing B
31	29	(30)	3	350	400	8	8	(X)	6	9	" "
32	30	(33)	2	600	700	6	12	(X)	8	10	" "
33	30	(32)	3	400	450	6	7	(X)	6	11	" "
34	30	(30)	2	400	400	20	6	X(7)	—	—	Patient about 7 mo pregnant
86	23	(23)	1	250	250	6	8	(X)	6	7	Continuing B; normal pregnancy; mid-forceps delivery
87	23	(24)	1	300	350	10	12	X(5)	—	—	Patient about 5 mo pregnant
88	23	(26)	1	350	400	12	8	X(3)	—	—	Patient about 3 mo pregnant; weight increase too rapid, advised lower calorie diet
89	23	(27)	2	400	400	8	5	(X)	7	4	Continuing B
90	23	(40)	1	300	450	30	—	—	—	—	Continuing B; couple desire no more children; male has coronary disease
91	23	(27)	1	400	350	7	9	X(M-3)	—	—	Patient miscarried at 13 wk; to recontinue B after first true menstrual period
92	23	(25)	2	350	400	5	8	(X)	6	9	Continuing B
93	23	(26)	3	450	400	9	7	(X)(C)	6.5	2	Continuing B; C = cesarean section; patient advised against further pregnancy
94	23	(24)	1	300	350	8	6	X(6)	—	—	Patient about 6 mo pregnant
95	23	(26)	2	400	450	6	10	X(4)	—	—	Patient about 4 mo pregnant; weight gain too rapid—advised obesity diet
96	23	(28)	2	250	350	10	8	X(3)	—	—	Patient about 3 mo pregnant; had staining past month; testosterone propionate and progesterone weekly injections; no staining past week
97	23	(26)	1	300	350	4	6	(X)	7	6	Continuing B; normal pregnancy; low forceps delivery
98	23	(25)	3	350	450	5	—	—	—	—	Patient not heard from since
99	23	(27)	1	250	300	7	4	X(5)	—	—	Patient about 5 mo pregnant
100	23	(29)	1	300	300	9	6	X(8)	—	—	Patient about 8 mo pregnant
101	23	(30)	2	300	400	7	10	(X)	8	3	Continuing B

TABLE 4—(*Continued*)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
102	24	(27)	2	300	350	27	—	—	—	—	Continuing Ⱥ; couple desire no more children; active pulmonary tuberculosis
103	24	(25)	3	300	400	4	5	(X)	6	8	Continuing Ⱥ
104	24	(25)	1	200	300	6	8	X(6)	—	—	Patient about 6 mo pregnant; previous history of husband being Rh +
105	24	(26)	2	250	250	9	6	X(3)	—	—	Patient about 3 mo pregnant
106	24	(27)	3	400	300	4	10	X(8)	—	—	Patient about 8 mo pregnant; overweight; diet; has subacute cholecystitis
107	24	(28)	2	350	400	7	6	(X)	7	5	Continuing Ⱥ; normal pregnancy; mid-forceps delivery
108	24	(28)	1	400	450	5	8	(X)	6.5	6	Continuing Ⱥ; normal pregnancy; breach delivery
109	24	(27)	2	350	300	8	5	X(4)	—	—	Patient about 4 mo pregnant
110	24	(26)	3	300	350	29	—	—	—	—	Continuing Ⱥ; couple desire no more children
111	24	(28)	2	250	400	8	9	(X)	7	5	Continuing Ⱥ
112	24	(27)	4	300	350	4	5	X(4)	—	—	Patient about 4 mo pregnant; past history toxemia during last 10 wk previous pregnancy
113	24	(29)	1	350	350	3	7	(X)	6	7	Continuing Ⱥ; staining during 6th mo; received progesterone injection weekly; stopped 2 wk after first injection; went on to normal delivery
114	24	(30)	3	400	500	5	8	X(5)	—	—	Patient about 5 mo pregnant; developed dinbetes insipidus 6 mo postpartum previous pregnancy
115	24	(28)	2	300	350	6	—	—	—	—	Patient not heard from since
116	24	(30)	3	400	550	10	5	(X)	8	3	Continuing Ⱥ; patient on obesity diet
117	24	(32)	1	250	400	5	10	(X)	6	7	Continuing Ⱥ; husband mild case of myxedema
118	25	(29)	2	300	350	19	—	—	—	—	Continuing Ⱥ; both previous pregnancies cesarean section; has been advised against further pregnancies
119	25	(27)	1	250	300	7	5	X(6)	—	—	Patient about 6 mo pregnant
120	25	(26)	1	200	250	6	8	X(3)	—	—	Patient about 3 mo pregnant; malnutrition problem
121	25	(28)	3	350	350	8	6	(X)	7	4	Continuing Ⱥ
122	25	(27)	2	300	400	5	7	X(5)	—	—	Patient about 5 mo pregnant
123	25	(30)	1	250	300	4	8	(X)	6	6	Continuing Ⱥ; acute appendectomy at 8 mo, uncomplicated; normal delivery
124	25	(25)	1	450	450	7	5	(X)	7	4	Continuing Ⱥ; both asthmatics and obese; obesity diet
125	25	(24)	4	400	350	27	—	—	—	—	Continuing Ⱥ; couple desire no more children
126	25	(26)	1	250	300	6	4	X(4)	—	—	Patient about 4 mo pregnant
127	25	(29)	3	400	350	6	—	—	—	—	Patient not heard from since
128	25	(28)	1	300	250	9	6	X(5)	—	—	Patient about 5 mo pregnant; weight increase too rapid; obesity diet
129	25	(29)	2	300	400	8	7	(X)	5.5	2	Continuing Ⱥ
130	25	(27)	3	400	500	5	6	X(7)	—	—	Patient about 7 mo pregnant; weight gain too rapid; obesity diet
131	25	(28)	1	300	300	10	8	X(4)	--	—	Patient about 4 mo pregnant; hypertension developed at end of 2nd mo
132	25	(30)	2	500	600	24	—	—	—	—	Continuing Ⱥ; both obese and asthmatic; desire no more children
133	25	(32)	3	350	350	9	11	(X)	7	3	Continuing Ⱥ; mid-forceps delivery
434	25	(31)	3	400	300	6	5	X(6)	—	—	Patient about 6 mo pregnant
135	25	(33)	1	300	450	4	8	(X)	6	5	Continuing Ⱥ
136	26	(25)	4	250	350	7	6	X(3)	—	—	Patient about 3 mo pregnant; fracture of right clavicle beginning of 3rd month; healing well
137	26	(27)	2	300	300	25	—	—	—	—	Continuing Ⱥ; husband was seriously injured; desire no more children

TABLE 4—(*Continued*)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
138	26	(26)	1	250	300	8	12	X(5)	—	—	Patient about 5 mo pregnant; moderate myxedema
139	26	(27)	1	450	400	5	9	(X)	6.5	4	Continuing Ḇ; last pregnancy delivered at 8 mo; infant normal
140	26	(27)	3	350	450	3	5	(X)	6	8	Continuing Ḇ; high forceps delivery
141	26	(28)	2	300	200	4	7	X(8)	—	—	Patient about 8 mo pregnant; ? toxemia: hypertension, 2+ albumen in urine, peripheral edema
142	26	(29)	1	250	350	6	10	X(4)	—	—	Patient about 4 mo pregnant; patient's infectious arthritis improved at end of second mo of pregnancy
143	26	(30)	2	350	400	7	6	(X)	7	10	Continuing Ḇ; patient had left pyelonephritis during 5th mo, which cleared after 6 wk; remaining pregnancy normal
144	26	(30)	3	450	550	21	—	—	—	—	Continuing Ḇ; because of husband's coronary condition couple desire no more children
145	26	(31)	2	300	300	6	—	—	—	—	Patient refused more pills, as she intended to become pregnant, but have heard no more since
146	26	(29)	1	300	350	4	6	X(6)	—	—	Patient about 6 mo pregnant; patient has rheumatic heart disease, with double mitral murmur
147	26	(30)	2	350	400	6	8	(X)	6	7	Continuing Ḇ
148	26	(28)	5	300	350	27	—	—	—	—	Continuing Ḇ; couple state they cannot afford more children
149	26	(31)	4	350	450	10	5	X(4)	—	—	Patient about 4 mo pregnant; male Rh negative during previous pregnancy of wife
150	26	(32)	2	400	450	9	6	(X)	7	4	Continuing Ḇ; patient has diabetes mellitus which flared up during 4th mo of previous pregnancy; did badly for 3 mo but developed no toxemia; high forceps delivery; advised against further pregnancy
151	26	(34)	1	350	400	5	7	(X)	8	9	Continuing Ḇ
152	27	(31)	2	350	350	6	—	—	—	—	Patient not heard from since
153	27	(30)	1	400	400	8	5	(X)	6	3	Continuing Ḇ; patient had hypertension in last 4 mo of pregnancy; normal delivery; warned against further pregnancies
154	27	(29)	3	300	400	23	—	—	—	—	Continuing Ḇ; couple desire no more children
155	27	(28)	3	250	350	8	8	X(3)	—	—	Patient about 5 mo pregnant
156	27	(28)	5	350	400	7	6	X(3)	—	—	Patient about 3 mo pregnant
157	27	(26)	4	350	350	5	6	(X)	5.5	7	Continuing Ḇ
158	27	(29)	2	300	450	7	8	(X)	6	3	Continuing Ḇ; patient stained 4 mo; given progesterone injections weekly; normal delivery
159	27	(29)	1	400	300	9	5	X(4)	—	—	Patient about 4 mo pregnant; weight gain too rapid; obesity diet
160	27	(30)	1	350	400	4	9	(X)	7	6	Continuing Ḇ
161	27	(29)	3	400	450	7	—	—	—	—	Husband killed in Korea
162	27	(31)	1	300	350	6	10	X(6)	—	—	Patient about 6 mo pregnant
163	27	(31)	2	450	400	9	7	(X)	5	4	Continuing Ḇ; patient obese; on diet
164	27	(32)	3	300	300	4	8	X(7)	—	—	Patient about 7 mo pregnant; stained first 4 mo; controlled on oral testosterone propionate
165	27	(33)	4	350	400	5	6	X(3)	—	—	Patient about 3 mo pregnant; has a furuncle of left labia; no glycosuria or hyperglycemia
166	27	(34)	1	400	500	9	8	X(5)	—	—	Patient about 5 mo pregnant; weight gain much too rapid; strict obesity diet

TABLE 4—(*Continued*)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
167	27	(35)	2	300	300	3	11	(X)	6	7	Continuing B
168	28	(31)	5	250	350	6	5	X(4)	—	—	Patient about 4 mo pregnant; patient's vitiligo flared and advanced with pregnancy
169	28	(34)	4	300	350	5	—	—	—	—	Patient not heard from since
170	28	(30)	2	350	400	8	6	X(M-3)	—	—	Patient miscarried in 12th wk; to resume B after first menstrual period
171	28	(30)	3	350	400	28	—	—	—	—	Continuing B; couple desire no more children
172	28	(29)	4	300	400	5	—	—	—	—	Patient not heard from since
173	28	(32)	2	400	450	7	8	(X)	7	5	Continuing B; obesity; advised obesity regime
174	28	(32)	1	300	350	5	7	(X)	6	8	Continuing B; low forceps delivery
175	28	(33)	2	250	300	9	6	X(6)	—	—	Patient about 6 mo pregnant; developed acute anterior poliomyelitis at 4th mo, no residual
176	28	(33)	1	400	450	6	7	(X)	8	7	Continuing B; patient had lobar pneumonia 5th mo; responded well to terramycin; remainder normal pregnancy; normal delivery
177	28	(33)	4	350	400	5.5	—	—	—	—	Patient not heard from since
178	28	(34)	2	300	450	7	5	(X)	6	4	Continuing B
179	28	(36)	1	400	500	4	8	X(7)	—	—	Patient about 7 mo pregnant; weight gain too rapid; obesity diet
180	28	(36)	4	300	400	10	6	X(3)	—	—	Patient about 3 mo pregnant
181	28	(34)	3	350	350	8	4	(X)	5	3	Continuing B
182	28	(31)	2	400	400	23	—	—	—	—	Continuing B; couple desire no more children
183	28	(35)	1	350	450	5	6	(X)	5.5	8	Continuing B
184	29	(29)	3	450	550	9	5	(X)	7	2	Continuing B; obesity regime
185	29	(30)	1	300	450	6	8	(X)	6	7	Continuing B; patient premature delivery at 8 mo; infant normal at 4 mo
186	29	(30)	5	350	300	3	4	X(5)	—	—	Patient about 5 mo pregnant; advised against further pregnancies
187	29	(33)	3	400	350	12	6	X(3)	—	—	Patient about 3 mo pregnant; has acute glomerular nephritis; watch closely
188	29	(31)	2	350	450	8	6	(X)	7	3	Continuing B
189	29	(34)	1	300	400	4	8	X(4)	—	—	Patient about 4 mo pregnant; nausea first 3 mo; controlled with B_6 injections biweekly
190	29	(27)	1	250	350	6	5	X(8)	—	—	Patient about 8 mo pregnant; membranes ruptured and draining watery discharge past 3 days
191	29	(35)	5	400	500	28	—	—	—	—	Continuing B; couple desire no more children
192	29	(33)	1	350	450	26	—	—	—	—	Continuing B; husband has carcinoma of colon; wife has pernicious anemia, controlled; couple desire no more children
193	29	(31)	6	300	350	4	7	X(6)	—	—	Patient about 6 mo pregnant; advised to go under constant B after this delivery
194	29	(35)	2	500	600	5	6	(X)(C)	7.5	5	Continuing B; *C* = cesarean section; obesity regime for both
195	29	(37)	3	300	400	3	5	X(3)	—	—	Patient about 3 mo pregnant; male has active pulmonary tuberculosis
196	29	(37)	2	300	300	4	8	(X)	6	4	Continuing B; previous delivery by low forceps
197	29	(35)	5	350	400	8	5	X(4)	—	—	Patient about 4 mo pregnant; patient had rubella at 2nd mo of pregnancy; no complications
198	29	(37)	1	400	500	7	9	(X)	7	2	Continuing B; male mild diabetic; on obesity-reducing regime
199	29	(37)	3	300	350	6	—	—	—	—	Wife killed in automobile accident
200	29	(39)	2	350	400	23	—	—	—	—	Continuing B; couple desire no more children

TABLE 4—(*Continued*)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
201	29	(39)	1	250	350	9	6	X[3]	—	—	Patient about 3 mo pregnant; patient mild diabetic, controlled
202	30	(33)	4	350	400	22	—	—	—	—	Continuing B; couple desire no more children
203	30	(31)	7	500	450	14	8	X[4]	—	—	Patient about 4 mo pregnant; on obesity diet; male has severe myxedema; advised continuous B after delivery
204	30	(32)	2	500	600	5	5	(X)[C]	8	4	Continuing B; *C* = cesarean section; obesity regime for both
205	30	(33)	3	400	500	20	—	—	—	—	Continuing B; patient has anterior pituitary mixed tumor; couple desire no more children
206	30	(36)	1	350	350	7	6	X[5]	—	—	Patient about 5 mo pregnant
207	30	(38)	5	300	400	6	—	—	—	—	Patient not heard from since
208	30	(37)	2	350	500	4	8	(X)	6	3	Continuing B
209	30	(38)	1	300	450	9	5	(X)	7	6	" "
210	30	(39)	4	400	450	5	6	(X)	6.5	6	" "
211	30	(40)	2	450	500	20	—	—	—	—	Continuing B; couple desire no more children; both on obesity regime
212	30	(36)	1	350	450	8	7	(X)	6	3	Continuing B
213	30	(40)	5	400	200	6	6	X[3]	—	—	Patient about 3 mo pregnant; male has carcinoma of prostate, controlled
214	30	(41)	4	350	550	18	—	—	—	—	Continuing B; couple desire no more children
215	30	(39)	2	300	350	7	11	(X)	8	4	Continuing B
216	30	(36)	3	350	450	26	—	—	—	—	Continuing B; couple desire no more children
217	30	(40)	1	300	400	5	8	X[6]	—	—	Patient about 6 mo pregnant; male has Rh negative blood

Daily therapeutic requirements were estimated in proportion to the weight level of the individual. Dosage was based on a unit of 5 mg of phosphorylated hesperidin for each kilogram of body weight, with an excess allowance to protect against possible loss through faulty absorption or excessive elimination. For example, a patient weighing 150 pounds (68 kg) would require 5 times 68, equal to 340 mg. The dosage given such a patient was 500 mg in divided doses—that is, 2 tablets of 100 mg each at breakfast, 1 tablet of 100 mg at lunch, and 2 tablets of 100 mg each at dinner. Earlier clinical experience had proved that concentration of the drug in the blood stream was a pertinent factor, and that a single daily dose would not maintain saturation. Because of the results obtained from animal experiments cited above, as well as from certain clinical experience to be described later, it was decided to administer medication to both male and female. All couples were therefore instructed emphatically that distribution of dosage with meals was essential if proper saturation was to be obtained. They were further advised that the medication must be taken by both male and female for 10 consecutive days to be certain of sustained adequate blood levels, in order that the antifertility effect could be assured. Also because of our clinical experience, they were cautioned that omission of medication by either partner for 48 hours would necessitate another consecutive 10-day period before antifertility action could be reestablished.

Although previous experience had indicated the nontoxicity of the drug, patients in the earlier groups who received more than 300 mg/24 hours were carefully watched for toxic symptoms. Particular attention was paid to blood changes, effects on the cardiorespiratory system, hepatic, renal, and metabolic functions, skeletal changes, bowel action, sleeping habits, nervousness, and irritability. The nontoxicity of the drug was further substantiated when a group of 15 couples, who had received up to 25 times the required oral dosage over a 10- to 50-day period, showed no toxic effects of any kind. Of this group of 15, five couples were given the drug intravenously in physiological saline solution, by the Murphy drip method, over 24-hour periods, two of the group receiving as much as 20,000 mg (20 g) in 24 hours for 10 consecutive days. No toxic manifestations or allergic reactions of any kind were encountered in any of these clinical studies.

The question of a clinical test that would serve as a guide in the administration of the drug was the next problem. Aside from saturation in the blood stream, no satisfactory test was found for the female. In the male, however, studies were made on fresh ejaculations for the presence of the enzyme hyaluronidase. The

TABLE 5

GROUP III—65 COUPLES (21.7%) AGES 31–37 (FEMALE)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
35	31	(30)	3	500	600	3	8	(X)	6	14	Continuing B; both overweight; put on obesity regime
36	31	(35)	1	450	450	16	8	X(5)	—	—	Patient about 5 mo pregnant; stained first 2 mo; controlled progesterone biweekly, parenterally
37	31	(33)	1	300	400	28	—	—	—	—	Continuing B; couple desire no more children
38	32	(35)	2	350	600	7	7	(X)	5	10	Continuing B; male hypertensive
39	32	(36)	1	450	500	8	8	(X)	6	9	Continuing B; obesity regime for both
40	33	(40)	1	450	600	21	4	X(4)	—	—	Patient about 4 mo pregnant; has hypertension; obesity regime for both
41	33	(38)	2	400	450	6	8	(X)	6	11	Continuing B
42	34	(35)	3	250	300	6	7	(X)	8	10	Continuing B; patient had bronchopneumonia 5th mo of pregnancy; responded to penicillin, aureomycin combination
43	36	(36)	2	400	500	4	8	(X)	5	13	Continuing B; high forceps delivery
44	37	(44)	3	400	400	28	—	—	—	—	Continuing B; male had cerebral accident; couple desire no more children
218	31	(32)	1	300	300	10	6	X(6)	—	—	Patient about 6 mo pregnant
219	31	(32)	2	250	300	7	5	(X)	6	10	Continuing B; low forceps delivery
220	31	(33)	2	400	500	8	7	(X)	12	7	Continuing B; obesity regime for both
221	31	(34)	3	350	400	29	—	—	—	—	Continuing B; male had acute coronary thrombosis; couple desire no more children
222	31	(33)	1	300	350	9	6	X(2)	—	—	Patient about 2 mo pregnant; ? staining past 2 wk; preventive parenteral testosterone propionate and progesterone biweekly
223	31	(35)	3	350	450	5	8	(X)	5	11	Continuing B
224	31	(37)	4	300	350	6	—	—	—	—	Patient not heard from since
225	31	(36)	2	350	350	8	8	X(4)	—	—	Patient about 4 mo pregnant; patient has hypertension, increased past mo
226	32	(35)	1	300	350	7	6	(X)	6	8	Continuing B; patient had staining 1st 3 mo, in previous pregnancy; controlled oral testosterone propionate; breach delivery
227	32	(35)	2	250	350	28	—	—	—	—	Continuing B; patient is severe hypertensive; couple desire no more children
228	32	(35)	3	300	400	24	6	X(3)	—	—	Patient about 3 mo pregnant; previous delivery was a placenta praevia
229	32	(37)	1	250	300	16	4	(X)(C)	11	2	Continuing B; C = cesarean section; advised to have no more pregnancies
230	32	(38)	2	400	350	5	—	—	—	—	Patient not heard from since
231	32	(39)	1	300	400	10	6	X(6)	—	—	Patient about 6 mo pregnant; fractured left wrist in 2nd mo; well-healed
232	32	(38)	3	350	350	9	8	(X)	6	7	Continuing B; patient has acute cholecystitis attacks
233	32	(31)	4	300	300	11	5	(X)	5	6	Continuing B; patient had lobar pneumonia 1st mo of pregnancy; responded to terramycin
234	33	(34)	2	350	450	12	6	X(5)	—	—	Patient about 5 mo pregnant
235	33	(40)	5	350	300	26	—	—	—	—	Continue B; patient has severe arthritis deformans; desires no more children
236	33	(33)	1	300	350	13	7	(X)	6	4	Continuing B
237	33	(35)	1	250	350	7	8	X(3)	—	—	Patient about 3 mo pregnant
238	33	(35)	3	350	300	5	6	(X)	5	10	Continuing B; patient has rheumatic heart disease, mitral regurgitation, aortic stenosis; well-compensated
239	33	(36)	2	300	400	11	8	X(7)	—	—	Patient about 7 mo pregnant

TABLE 5—(*Continued*)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
240	33	(30)	4	250	300	12	6	(X)	4	5	Continuing B; patient had acute anterior poliomyelitis, 4th mo preganacy; left with no residual
241	34	(35)	2	300	350	9	7	(X)	5	7	Continuing B
242	34	(37)	4	350	400	13	6	X(3)	—	—	Patient about 5 mo pregnant; had acute left pyelonephritis, beginning 4th mo
243	34	(39)	3	300	350	5.5	—	—	—	—	Patient not heard from since
244	34	(38)	2	250	300	13	6	X(3)	—	—	Patient about 3 mo pregnant; has mild Simmonds' disease
245	34	(38)	5	300	400	17	—	—	—	—	Continuing B; patient has severe diabetes mellitus; desires no more children
246	34	(39)	1	350	300	14	8	(X)	4	3	Continuing B
247	34	(40)	1	300	400	4	6	(X)(P)	5	4	Continuing B; patient delivered prematurely 8th mo by high forceps; infant normal weight 3rd mo
248	34	(41)	2	400	350	21	—	—	—	—	Continuing B; couple desire no more children
249	35	(35)	4	300	300	16	12	X(7)	—	—	Patient about 7 mo pregnant; has pernicious anemia, controlled, with B_{12}
250	35	(36)	3	300	400	15	8	X(4)	—	—	Patient about 4 mo pregnant
251	35	(37)	2	350	350	20	—	—	—	—	Continuing B; can afford no more children
252	35	(39)	1	300	300	10	7	(X)	6	3	Continuing B; delivery by version
253	35	(40)	1	250	300	4.5	—	—	—	—	Both killed in automobile accident
254	35	(40)	2	300	350	5	6	(X)	5	4	Continuing B
255	35	(39)	3	350	300	12	11	X(8)	—	—	Patient about 8 mo pregnant; has had bleeding duodenal ulcer 5 mo
256	35	(41)	5	300	400	15	4	X(5)	—	—	Patient about 5 mo pregnant; male has severe diabetes mellitus, controlled; advised continuous B after this pregnancy
257	36	(40)	2	350	300	4	10	(X)	6	5	Continuing B
258	36	(51)	1	300	350	3	6	(X)	5	6	Continuing B; male has carcinoma of tongue
259	36	(39)	2	400	500	10	8	X(4)	—	—	Patient about 4 mo pregnant; has mild hypertension; slight increase past mo
260	36	(40)	3	300	350	9	9	X(7)	—	—	Patient about 7 mo pregnant; staining for 10 wk beginning of 3rd mo; parenteral progesterone biweekly
261	36	(39)	4	300	400	18	—	—	—	—	Continuing B; patient has severe diabetes mellitus; desire no more children
262	36	(38)	3	350	300	7	6	(X)	4	4	Continuing B
263	36	(40)	2	400	450	8	5	(X)	6	7	Continuing B; both on obesity regime
264	36	(39)	2	300	400	6	—	—	—	—	Patient not heard from since
265	37	(43)	1	350	450	5	6	(X)	5	8	Continuing B; patient had pertussis 2 mo previously
266	37	(41)	1	400	450	8	12	X(6)	—	—	Patient about 6 mo pregnant; had acute appendectomy 3rd mo pregnancy; recuperated quickly
267	37	(45)	1	300	350	14	—	—	—	—	Continuing B; couple desire no more children
268	37	(43)	2	350	400	12	8	X(5)	—	—	Patient about 5 mo pregnant; appendectomy 2nd mo; no complications
269	37	(44)	1	300	300	8	10	(X)	5	7	Continuing B; delivery mid-forceps; bad varicosities of legs
270	37	(42)	3	300	350	5	—	—	—	—	Patient not heard from since
271	37	(42)	1	350	400	9	6	X(2)	—	—	Patient about 2 mo pregnant; history toxemia last 3 mo of 1st pregnancy
272	37	(48)	1	250	300	11	—	—	—	—	Continuing B; male has bronchiogenic carcinoma of lung (right); couple desire no more children

usual studies were made: sperm count, percentage motility, percentage morphology, and total volume. An estimate of hyaluronidase in turbidity-reducing units (TRU) after the method of Nodine and Perloff (*10*)

TABLE 6

GROUP IV—19 COUPLES (6.3%) AGES 38–40 (FEMALE)

Case No. (couples)	Ages F	Ages (M)	Previous pregnancy	Total daily dosage (mg) F	Total daily dosage (mg) M	Fertility control period (months)	Fertilization time (weeks)	Pregnancy and delivery	Postpartum interval (weeks)	Secondary control period (months)	Remarks
45	38	(37)	1	350	600	6	7	(X)	5	11	Continuing Ⱥ
46	39	(40)	3	450	500	7	11	(X)	12	6	Continuing Ⱥ; low forceps delivery; patient has hypertrophic and infectious arthritis
47	40	(45)	1	350	450	16	—	—	—	—	Continuing Ⱥ; couple desire no more children
48	40	(51)	2	600	800	8	8	(X)	6	5	Continuing Ⱥ; both on obesity regime
273	38	(39)	3	300	350	29	—	—	—	—	Continuing Ⱥ; couple desire no more children
274	38	(41)	5	350	350	25	—	—	—	—	Continuing Ⱥ; severe arthritis; couple desire no more children
275	38	(45)	1	300	400	10	12	(X)	5	6	Continuing Ⱥ
276	38	(47)	3	350	300	28	—	—	—	—	Continuing Ⱥ; couple desire no more children
277	38	(49)	2	400	450	8	6	X(6)	—	—	Patient about 6 mo pregnant; stained 1st 2 mo; control oral testosterone propionate
278	39	(43)	1	350	400	8	9	(X)	4	9	Continuing Ⱥ; acute pleurisy (left) 6th mo of previous pregnancy
279	39	(37)	1	300	350	24	—	—	—	—	Continuing Ⱥ; patient burnt in holocaust
280	39	(44)	2	350	400	6	—	—	—	—	Patient not heard from since
281	39	(47)	1	350	350	26	—	—	—	—	Continuing Ⱥ; couple desire no more children
282	39	(50)	1	400	500	5	7	(X)	6	10	Continuing Ⱥ; delivered by low forceps
283	40	(41)	3	450	400	7	8	(X)	6	8	Continuing Ⱥ; moderate diabetes mellitus, controlled
284	40	(44)	2	300	350	11	6	X(5)	—	—	Patient about 5 mo pregnant; mild diabetic; controlled on diet
285	40	(46)	4	350	400	30	—	—	—	—	Continuing Ⱥ; couple desire no more children
286	40	(49)	2	300	350	8	11	X(4)	—	—	Patient about 4 mo pregnant; has acute cholecystitis
287	40	(51)	2	400	450	29	—	—	—	—	Continuing Ⱥ; couple desire no more children
						GROUP V—15 COUPLES (5%) AGES 41–43 (FEMALE)					
49	41	(44)	2	600	500	29	—	—	—	—	Continuing Ⱥ; couples desire no more children
50	43	(49)	4	250	250	30	—	—	—	—	
288	41	(42)	3	300	350	20	—	—	—	—	
289	41	(40)	2	350	400	23	—	—	—	—	
290	41	(43)	4	400	500	23	—	—	—	—	
291	41	(46)	3	500	550	25	—	—	—	—	
292	41	(50)	1	450	400	17	12	X(7)	—	—	Patient about 7 mo pregnant; severe bronchial asthmatic
293	42	(51)	5	500	600	25	—	—	—	—	Continuing Ⱥ; couples desire no more children
294	42	(51)	3	450	500	26	—	—	—	—	
295	42	(52)	6	300	400	26	—	—	—	—	
296	42	(53)	2	400	500	27	—	—	—	—	
297	43	(54)	1	400	450	27	—	—	—	—	
298	43	(54)	5	500	600	28	—	—	—	—	
299	43	(55)	4	400	500	28	—	—	—	—	
300	43	(58)	3	350	450	29	—	—	—	—	

was recorded. This study in itself was extremely interesting and explains some of the discrepancies found in the animal experiment. However, discussion of these findings involves extensive material that cannot be included in the present communication; it will be reported completely in a subsequent publication.

A comparative study was made of the incidence of coitus before and during therapy. On questioning the female, one significant fact was revealed. Many of those who had been using mechanical devices showed a definite increase in total orgasm when the oral therapy was used. From this observation it may be deduced that mechanical methods had produced a state of anxiety causing varying degrees of frigidity, which

resulted in a loss of total orgasm. A significant increase in the frequency of coitus was found in this group. Interestingly enough, it was discovered that the frequency pattern now practiced by these couples corresponded essentially to the frequency pattern practiced in the early months of their marriage.

Statistical Case Analysis

The 300 couples reported are divided into five age groups according to the reproductive years. The age of the female provides the basis for classification. Of this group:

I. 43 couples (14.3%) varied in age from 17 to 22 years (Table 3).
II. 158 couples (52.6%) varied from 23 to 30 years (Table 4).
III. 65 couples (21.7%) varied from 31 to 37 years (Table 5).
IV. 19 couples (6.3%) varied from 38 to 40 years (Table 6).
V. 15 couples (5%) varied from 41 to 43 years (Table 6).

In Group I, 25 couples have had 1 normal pregnancy with normal delivery and normally developed child; 11 have had 2 normal children; 6 have had 3; 1 has had 4. In Group II, 59 couples have had 1 normal child; 47 have had 2 children; 29 have had 3; 13, 4; 8, 5; 1, 6; and 1 has had 7. Of Group III, 22 couples have had 1 child; 20 have had 2 children; 14, 3; 6, 4; 3, 5. Of Group IV, 7 couples have had 1 normal child; 6 have had 2 children; 4, 3; 1, 4; and 1 has had 5. Of Group V, 2 couples have had 1 child; 3 have had 2; 4, 3; 3, 4; 2, 5; and 1 has had 6. The interval from the end of the last postpartum to the beginning of the fertility control period varied from 2 to 21 months. Breast-fed infants averaged 25.2 per cent. Periods of breast-feeding varied from 2 weeks to 6 months.

All couples who terminated fertility control did so voluntarily for the purpose of having a wanted child, with the exception of three cases, which will be discussed later. The shortest period of fertility control was 3 months; the longest period was 30 months. Of the entire group of 300 couples, 21 females from Group I, 69 from Group II, 27 from Group III, and 6 from Group IV (total 123, 41 per cent) have had a period of fertility control followed by a normal pregnancy, and repeated therapy for a second period of control after the first menstrual period postpartum. Secondary periods of fertility control varied from 2 to 14 months. Ninety-seven couples (32.3 per cent) have gone through a period of control and are now in varying stages of pregnancy. Of these there were 14 in Group I, 57 in Group II, 21 in Group III, 4 in Group IV, and 1 in Group V. Sixty couples (20 per cent) were controlled continuously up to 30 months. The remaining 20 couples (6.7 per cent) were controlled for periods up to 6 months but were not heard from thereafter.

The total woman-years of protection for the 300 cases was 317.1—247.6 in the first control period and 69.5 in the secondary control period. The two control periods, giving the grand total of 317.1 woman-years, yield a figure far above the American Medical Association standard of 200 woman-years for any group studied for 12 months.

No couple in the entire group of 220 pregnancies reported any difficulty in impregnation. The longest period required for conception was 9–13 weeks, of which there were 31 cases; 179 couples reported a 5- to 8-week interval, and 10 reported impregnation after the first menstrual period following omission of medication. The incidence of miscarriage, premature births, and cesarean section was as follows: 3 miscarriages at 12–13 weeks; 5 premature births at 7½–8 months; and 5 cesarean sections. All other pregnancies, deliveries, and postpartum periods were normal. Babies born to these couples were all healthy, normal specimens. Breast-fed babies averaged 39.5 per cent. Periods of breast-feeding varied from 4 weeks to 6 months.

Two couples who had experienced a long period of questionable sterility prior to this therapy surprisingly fell into the group of 10 cases requiring but one cycle for impregnation. As mentioned previously, they had been deliberately selected for the experiment because of their history of one normal child, followed by a long period of apparent sterility, although both husband and wife had been declared normally fertile by competent urologists and obstetricians. Apparently some correction may have occurred, which suggests the possibility that phosphorylated hesperidin may possess fertility-stimulating, as well as antifertility, activity. However, further study is essential before a definite explanation can be elicited.[4]

Discussion and Conclusions

In the present study of 300 married couples the antifertility action of the drug was complete except for the two cases described. The two so-called failures are of no scientific significance, because of the lack of cooperation of the couples, as revealed by our method of dispensing medication. The tablets were bottled in lots of 100, each bottle recorded on a tally card for the patient to whom it was given, with the date and dosage for that patient. No one but members of the office staff dispensed the tablets. When a patient applied for more tablets he was required to return any remaining from the previous lot. Before more tablets were dispensed, a tally was made against the previous date and daily dosage. The number of tablets returned plus the number calculated should be equal to the total number dispensed for that period.

For example, in tallying the intake of the first so-called failure, there was a discrepancy of 200 tablets in the male and 160 tablets in the female. This was consistent with a 40-day dosage of 500 mg/24 hours for the husband, and 40 days at 400 mg/24 hours for the wife. Confronted with this information, the couple ad-

[4] Since writing this report an additional case has been seen—that of a 26-year-old female who had been having anovulatory cycles—which seems to fall into this possible group. Observations on these cases will be reported in a later communication.

mitted they had not taken their medication during a 40-day Rocky Mountain tour. The second failure showed a discrepancy of some 110 tablets, and upon careful questioning the couple admitted that during a drinking spree lasting 7 days neither member had followed the prescribed therapy.

Eighteen other patients in this group of 300 showed discrepancies varying up to 46 tablets in one individual—the male member of one couple. These omissions, however, were sporadic over a 90-day period, during which not more than 2 tablets had been omitted in any 24-hour period. The remaining tablets were accounted for by irregular omissions of not more than one 100-mg tablet from a total of 600 mg in a 24-hour period. Instructions were followed precisely by the remaining 280 cases, resulting in a 100 per cent check of all tallies.

The necessity of divided dosage over a 24-hour period has been mentioned. This was important to establish a blood saturation level, which remained fairly constant over a 24-hour period. Experience has proved that the drug is best administered with meals; where necessary, a fourth dose can be given at bedtime. The author's general rule was to prescribe four doses for the wife, and three doses for the husband during the 24-hour period. A constant observation in all couples taking this medication was the lack of rebellion against taking the medication in divided doses. Patients who have been opposed to taking pills all their lives seemed willing to take this factor. It is most important to impress upon the couples this distribution of dosage, as success depends upon the blood saturation.

This drug is an oral medication, physiological in action, which can be taken indefinitely without toxic effects or permanent inhibition of fertility. The medication must be taken for 10 consecutive days by both partners before antifertility action can be assured, and thereafter continuously by both partners at the prescribed daily divided dose. Fertility can be restored merely by omitting the drug for a 48-hour period. Should medication be omitted for 48 hours by either member of the couple, the 10 consecutive days of therapy must be repeated by both partners in order to re-establish fertility control. Following pregnancy, these 10 consecutive days of medication should not be started until after the first menstrual period postpartum. Phosphorylated hesperidin has been given clinically along with other substitution factors, such as vitamins, endocrines, amphetamine derivatives, and decholic acid derivatives without apparent interference in its action. As has been shown in both the text and tables, its antifertility action is not inhibited by trauma, infectious diseases, or systemic diseases. Again a word of warning must be expressed—it must be remembered that only one specific radical of this drug, phosphorylated hesperidin, has antifertility activity.

It must be realized that this preliminary report is presented for its experimental value only. Much more clinical data must be accumulated before the general use of this antifertility factor is warranted.

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News and Notes

Symposium on Phosphorus Metabolism, Part II

The second Symposium on Phosphorus Metabolism, sponsored by the McCollum-Pratt Institute, was held at The Johns Hopkins University, Baltimore, June 16–19, 1952. Part I of this symposium was held a year ago, and this sequel provided an opportunity for discussion of those aspects not covered or only briefly treated in Part I.

The program started with a discussion of Phosphate Assimilation, with formal presentations by D. M. Greenberg, who covered the animal metabolic aspect, and by P. K. Stumpf, who dealt with plant metabolism. The second session considered the Role of Phosphate in Amino Acid and Protein Metabolism, and formal papers were presented on the following subjects: Enzymatic Synthesis of Glutathione, by K. Bloch; Transpeptidation and Transamidation Reactions, by C. S. Hanes; Synthesis and Transfer of Labile Methyl Groups, by G. Cantoni; Genetic Control of Enzyme Formation, by D. Bonner; and Enzymatic Dephosphorylation of Phosphoproteins and the Nature of Phosphorus Linkages, by G. Perlmann. Session III, dealing with the Role of Phosphorus in the Metabolism of Lipids, consisted of papers on The Chemistry of Phospholipids, by J. Folch-Pi; Formation of Phospholipids in Animal Tissues, by C. Artom, and The Enzymatic Oxidation of Fatty Acids, by E. D. Kennedy. The Chemistry and Metabolism of Nucleic Acids, the topic for Session IV, included the follow presentations: The Products of Nucleic Acid Hydrolysis and their Relationship to its Structure, by E. Volkin; Newer Aspects of the Chemistry of Nucleic Acids, by S. Zamenhof; Metabolism of Nucleic Acids in Microorganisms, by J. O.

Lampen; Biosynthesis of Nucleic Acids, by G. B. Brown; and The Role of Desoxyribonucleates in Bacterial Transformation, by R. Hotchkiss. Session V, on The Role of Phosphate in the Metabolism of Photosynthetic and Chemoautotrophic Organisms, consisted of the following papers: Phosphorus Compounds in Photosynthesis, by M. Calvin; Reduction of Pyridine Nucleotides in Photosynthesis, by W. Vischniac; and Serendipic Aspects of Recent Nutritional Research in Bacterial Photosynthesis, by M. Kamen. Session VI, which was concerned with the Influence of Hormones on Phosphate Metabolism, included the following papers: The Effects of Epinephrine and the Hyperglycemic Factor on Liver and Muscle Metabolism *in vitro*, by E. Sutherland; Metabolic Effects of the Thyroid Hormone, by C. H. Du Toit; Function of the Parathyroid, by J. Aub; and The Effects of Adrenal Cortical and Pituitary Hormones, by C. R. Park. Phosphate Metabolism in Specialized Tissues, the subject of the final session, VII, was developed by papers on Pathways of Phosphate Metabolism in Cancer Tissue, by V. R. Potter; Skeletal Metabolism of Phosphorus, by W. Armstrong; Metabolic Aspects of Renal Tubular Transport, by J. V. Taggart; The Role of Phosphate in the Maintenance of Membrane Potential and Selective Ionic Accumulation in Muscle Cells, by G. Ling; and Spatial and Chemical Exchange of Phosphate in the Resting and Active Nervous System, by R. Tschirgi.

Sixty-five invited discussants, all of them active investigators in the different fields, offered critical comments on the papers that were, in general, spirited and pertinent. Although the main theme of the symposium necessitated broad coverage of the many different aspects of phosphorus metabolism, it served on the whole to emphasize the need to integrate and unify the many fundamental interrelationships in these areas of biochemistry. It can be confidently predicted that the volume containing the papers in this symposium will equal the high standards set by the first volume, and that the two will represent a most valuable comprehensive and critical review of the subject of phosphorus metabolism.

The committee in charge of the symposium is again to be congratulated, not only for arranging an excellent scientific program, but also for providing excellent facilities and accommodations. Although not a part of the official program, one of the interesting extracurricular events was the historical survey of the development of biochemistry and personal recollections by E. V. McCollum at the banquet.

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Scientists in the News

P. Allen, sedimentary petrologist and lecturer in the Department of Geology at Cambridge University, has been appointed to the chair of geology at the University of Reading, made vacant by the retirement of **H. L. Hawkins,** who has been at Reading since 1909.

Odin W. Anderson has been appointed director of research for Health Information Foundation, of New York. The foundation's research program includes studies on methods of payment for medical care, community self-surveys of health facilities and services, medical public relations, and child health. Dr. Anderson has been on the faculty of the University of Western Ontario as associate professor in the socioeconomic aspects of medicine.

William L. Batt, minister in charge of the ECA mission to the United Kingdom, and formerly president of SKF Industries, Inc., has been awarded the Howard Coonley Medal for distinguished service in the standardization movement, administered by the American Standards Association. Mr. Batt has been associated with SKF for 45 years and was its president, 1922–51.

William H. P. Blandy, president of Health Information Foundation, addressed the sixth general assembly of the World Medical Association in Athens, on "Information, the Key to Health."

J. Russell Bright, associate director of the Division of Contract Services and professor of chemistry at Wayne University, has been appointed representative of his institution on the Council of Participating Institutions of Argonne National Laboratory. Wayne University was recently elected the thirty-second participating institution of the laboratory.

James E. Chapman retired July 1 from the New Mexico College of Agriculture and Mechanic Arts, where he was assistant professor of agronomy. **Merrill R. Pack** succeeds him. Mr. Chapman has located in Miamisburg, Ohio.

Gardner H. Chidester, chief of the Pulp and Paper Division, U. S. Forest Products Laboratory, has been assigned to work with the Forestry Division of FAO in Rome. Mr. Chidester will be on special assignment with the UN organization for three months. He has been asked to help FAO consider ways of meeting the worldwide need for pulp and paper, particularly newsprint.

Gregory S. Duboff, who has been director of research for the Emery Tumor Group, of Los Angeles, has been appointed director of the Bio-Physics Research Institute of the same city. The institute is being established as a conference of specialists for the application of highly specialized devices and newer methods of research in cancer.

V. C. A. Ferraro, until recently at University College, Exeter, has been appointed professor at Queen Mary College, University of London, to take the place of **G. C. McVittie,** who is now at the University

of Illinois. Professor Ferraro was appointed in 1947 to the newly created chair of applied mathematics in University College. In 1948 he spent some months on leave as a guest investigator at the Department of Terrestrial Magnetism of the Carnegie Institution of Washington and in the succeeding year he delivered a course of lectures on solar and cosmic magnetism at the Royal Observatory of Belgium. Dr. Ferraro is probably best known for his work in conjunction with S. Chapman on the theory of magnetic storms and the aurora.

Dorothy A. E. Garrod has resigned from the Disney professorship of archaeology in the University of Cambridge to carry on excavations in western France. Professor Garrod was appointed to the Disney chair in 1939, but spent much of the war period analyzing air photographs for the RAF. **Grahame Clark**, who succeeds her, is a graduate of the Cambridge "school" and is at present lecturer there. His interest in the Stone Age started while at Marlborough College, and for the past few years he has been conducting excavations at Star Carr, near Scarborough, which have revolutionized our knowledge of the Mesolithic settlement in northeastern England.

John Gurland, formerly with the Cowles Commission and the Committee on Statistics of the University of Chicago, has joined the staff of the Statistical Laboratory of Iowa State College. He will teach courses in statistics in the graduate college and engage in research and consulting.

Edwin L. Gustus, vice president in charge of the Chicago office of the Bjorksten Research Laboratories, is in Europe to review research programs and problems with several of the firm's European clients before returning to Chicago late in the year. His itinerary will include the major countries of Western Europe, as well as the Near East.

Marshall C. Harrington has been granted a year's leave of absence from his teaching duties at Drew University to accept an appointment under Unesco's program of technical assistance to underdeveloped nations. Dr. Harrington, who has headed Drew's Physics Department since 1931, will serve as professor of physics in the University College at Bagdad. In the Unesco assignment he will succeed one of his former students, **Albert V. Baez,** professor of physics at the University of Redlands, in California.

Merritt L. Kastens has been appointed assistant to the director of Stanford Research Institute. With *Chemical and Engineering News*, and *Industrial & Engineering Chemistry* since 1946, Mr. Kastens was associate editor at the time of his resignation.

Thomas Lauritsen, Caltech associate professor of physics, has left for Denmark to lecture and conduct research in experimental physics at Niels Bohr's Institute for Theoretical Physics at the University of Copenhagen. The trip and lectureship are being made under a U. S. Educational Exchange grant awarded under provisions of the Fulbright Act.

Howard J. Lucas, professor of organic chemistry at the California Institute of Technology, has been named winner of the 1953 Scientific Apparatus Makers Award in Chemical Education. The award will be presented at the national American Chemical Society meeting in Los Angeles next March, at which time Dr. Lucas will address the Division of Chemical Education. The award was established in 1950 by the association "to recognize outstanding contributions to chemical education." For nearly 40 years Dr. Lucas has been in charge of the undergraduate course in organic chemistry at Caltech.

Samuel L. Meyer, professor and head of the Department of Botany at Florida State University, has been appointed executive director of the American Institute of Biological Sciences and executive secretary of the Division of Biology and Agriculture of the National Research Council. Dr. Meyer is on leave of absence from his post at the university.

John M. Miller, who retired last June as deputy director of the Naval Research Laboratory, has been named the recipient of the Institute of Radio Engineers' Medal of Honor for 1953, and the 1953 Morris Liebmann Memorial Prize, given annually by the institute for a recent important contribution to the radio art, went to **John A. Pierce,** senior research fellow at Harvard University. Mr. Pierce is known for his contributions to the development of the loran system of long-range radio navigation which was widely used by the armed services during World War II, and more recently for his conception of the radux system of long-range navigation now under development for the government. **Frank Gray,** research engineer of Bell Telephone Laboratories, Murray Hill, N. J., was awarded the Vladimir K. Zworykin Television Prize Award for 1953, given annually by the institute for an outstanding contribution to television. The presentation of awards will be made during the annual meeting in New York on Mar. 25.

Robert A. Patton has been appointed professor of psychology and chairman of the department at the University of Pittsburgh. He has been associated with the staff of the Psychology Department for more than ten years and has been a member of the research staff of the Western Psychiatric Institute and Clinic in the university's Medical Center. **Jack Matthews,** associate professor of psychology, has been named director of the division of psychological services. The appointments of Drs. Patton and Matthews follow the retirement from the psychology staff of **Carroll Whitmer,** who was head of the division of psychological services and who has been serving as acting head of the department. Dr. Whitmer has accepted a position as head psychologist of the new VA Hospital at Salt Lake City.

J. Donald Ryan has been appointed instructor in the Department of Geology at Lehigh University.

F. Sanger, of the University of Cambridge, will spend the month of November at Northwestern Uni-

versity as a visiting lecturer. In addition to a special lecture on the determination of the sequence of amino acids in insulin, he will deliver a series of talks on "The Chemistry of Proteins" as part of a graduate course in biochemistry.

Elmer L. Shaffer has been appointed director of laboratories of the New Jersey State Department of Health. Dr. Shaffer was formerly senior histologist in charge of the Bureau of Pathology of the State Department of Health.

James A. Shannon has been appointed associate director of the National Institutes of Health, U. S. Public Health Service, succeeding **Norman H. Topping,** whose appointment as vice president in charge of medical affairs at the University of Pennsylvania becomes effective Nov. 1. For the past three and one half years, Dr. Shannon has served as associate director of the National Heart Institute. In his new post, which carries the rank of assistant surgeon general, Dr. Shannon will coordinate the medical research program conducted in the laboratories of the seven institutes that comprise NIH. Before joining NHI in 1949, Dr. Shannon served for three years as director of the Squibb Institute for Medical Research.

P. A. Sweet, who has been at the University of Glasgow, has been appointed assistant director of the University of London Observatory at Mill Hill, the director of which is C. W. Allen. Dr. Sweet will be concerned with theoretical astronomy; his special interest has been in problems of cosmic magnetic fields.

William E. Taylor has been named research physicist in charge of the Phoenix Arizona Motorola Research Laboratory transistor and semiconductor research. Prior to his assignment to Motorola's Solid State Physics Research activity, Dr. Taylor was associated with the University of Tennessee, the Oak Ridge National Laboratory, and Purdue University.

Education

C. J. Gorter, professor of physics at the University of Leiden, recently gave a series of three special lectures at **California Institute of Technology.** In addition to discussing the history and the research program of the Kamerlingh Onnes Laboratory, of which he is director, Dr. Gorter spoke on "Paramagnetic Relaxation and Resonance" and "Aligning Atomic Nuclei."

Carnegie Institute of Technology has dedicated its new building for the Graduate School of Industrial Administration, which was founded in 1949 with a gift from the Mellon Foundation. Aim of the school is the training of young men for management positions; because of the teaching methods only a small number of students are admitted each year.

At the dedication of the new Life Sciences Building at **Colby College** in October, William K. Gregory, formerly of Columbia University and the American Museum of Natural History, presented a series of five lectures on "Interacting Factors of Human Comprehension and Behavior."

New York University opened this month the Wallace Clark Center for International Management, established by a gift of Mrs. Clark. The center will include facilities for seminars and conferences and the management library containing foreign reports and records acquired by the late Mr. Clark.

Northwestern University Medical School is presenting a series of lectures on problems and phases of cancer and cancer treatment and progress to date on Wednesday evenings. The first lecture was given on Oct. 6 by Shields Warren. Other speakers will be Cornelius P. Rhoads, Raymond F. Kaiser, John J. Bittner, Wendell M. Stanley, Emil Novak, Van R. Potter, Granville A. Bennett, Edward D. Churchill, and Albert Tannenbaum.

Grants and Fellowships

The **American Association of University Women** offers 25 fellowships for advanced study or research during 1953–54, ranging from $1500 to $3000. Applications and supporting materials must reach the Secretary, Committee on Fellowship Awards, AAUW, 1634 I St., N.W., Washington 6, D. C., by *Dec. 15.*

The **American Cancer Society Clinical Fellowships and Traineeships** will continue through the next institutional year, July 1–June 30, with fellowship training beginning on July 1. The traineeships are opportunities for training for physicians at a level somewhat lower than the fellowships and carry stipends up to a maximum of $3600, at which level the physician will be designated as a clinical fellow. Fellow- and traineeships will be made available primarily to teaching institutions approved by the AMA Council on Medical Education and Hospitals. Deadline for filing applications is *Nov. 10*; for complete information write to Brewster S. Miller, Professional Education Section, 47 Beaver St., New York 4.

The **Arctic Institute of North America** is offering research grants for scientific field investigations in North America or studies at one of the institute offices. Application forms, which must be completed by *Dec. 1,* may be obtained from the institute, 3485 University St., Montreal, Canada, or 1530 P St., N.W., Washington, D. C.

The **John Hay Whitney Foundation,** 30 Rockefeller Plaza, New York 20, will accept applications until *Dec. 15* for fellowships for graduate work in the humanities. Qualified teachers from Maine, New Hampshire, Vermont, Alabama, Arkansas, Florida, Louisiana, Mississippi, Illinois, Indiana, Iowa, Missouri, Idaho, Montana, Utah, and Wyoming will be selected to attend Columbia or Yale during 1953–54, with full salary, tuition, and transportation paid. Each teacher accepted as a John Hay Fellow is granted a year's leave by his employing school system and agrees to return following his university work.

Miscellaneous

Among those who will receive awards at the Medal Day ceremonies of The **Franklin Institute** (SCIENCE, 116, 315 [1952]) are Albert J. Williams, Jr., associate director of research with Leeds & Northrup Co., Philadelphia—a John Price Wetherill Medal for his invention of the Speedomax self-balancing recorder; Arthur M. Stoner, vice president in charge of engineering, of the Jacobs Manufacturing Co., West Hartford, Conn.—Certificate of Merit for his development of machine tool chucks; Edwin Loy Hall, director of the testing laboratories of the American Gas Association, Inc.—a Walton Clark Medal for his contributions and inventions in processes of gas manufacture; Edward C. Molina, of the Newark College of Engineering—an Elliott Cresson Medal for his contributions and inventions in the improvement of telephonic communications; Wolfgang Pauli, of the Physikal. Institut of the Eidgenössische Technische Hochschule, Zurich—the Franklin Medal for his work in atomic physics and specifically for his formulation of the exclusion principle.

Recent Deaths

Henry L. Alves (59), of San Francisco, chemist, Dunsmuir, Calif., Aug. 24; **Roger W. Armstrong** (72), civil engineer, Basking Ridge, N. J., Aug. 24; **Jean E. Chalanqui Beuret** (79), civil engineer, Buenos Aires, Aug. 20; **Isaac Bildersee** (65), of Brooklyn, educator, Star Lake, N. Y., Aug. 23; **E. W. Bodine** (46), plant pathologist, San Francisco, Aug. 11; **Robert L. Bucher** (57), chest specialist, Philadelphia, Sept. 14; **Jeremias Cardenas** (81), educator, Pelham, N. Y., Aug. 30; **Jack W. Clark** (37), of Ontario, Calif., geologist and mineralogist, Tananarive, Madagascar, Aug. 8; **Charles A. E. Codman** (83), of Philadelphia, physician, Camden, Me., Aug. 31; **Melville T. Cook** (83), plant pathologist, Washington, D. C., Aug. 11; **Ann M. A. Ellis** (38), of Clinton, N. Y., home economist, Utica, N. Y., Sept. 15.

Harry J. Fehr (66), of Philadelphia, eye, ear, nose, and throat specialist, Marlton, N. J., Sept. 15; **Royal H. Fowler** (69), surgeon, Glen Ridge, N. J., Aug. 31; **Hugh J. Fraser** (54), of Larchmont, N. Y., metallurgical and mining engineer, Montreal, Aug. 22; **Augustin Frigon** (64), director of planning and research, Canadian Broadcasting Corp., Ottawa, July 9; **Mario C. Giannini** (50), of New York, mechanical engineer, Winter Park, Fla., Aug. 24; **Manfred L. Gorten** (66), neurologist and psychiatrist, Newark, N. J., Aug. 31; **Richard Gregory** (88), physicist, meteorologist, astronomer, and editor, former president, British Association for the Advancement of Science, Middleton, Eng., Sept. 15; **A. T. Hanritta** (49), of Austin, Tex., psychiatrist, Boston, Aug. 23; **Charles Hire** (54), physicist, Bloomington, Ind., Sept. 9; **B. Smith Hopkins, Sr.** (79), chemist, Champaign, Ill., Aug. 27; **Clarence M. Hyland** (66), chemist, Apple Valley, Calif., Aug. 28.

Alfred Japha (81), pediatrician and tuberculosis specialist, Denver, Sept. 3; **Otto K. Kaspereit** (69), optical engineer, Philadelphia, Sept. 18; **Sherman L. Kelly** (—), inventor and engineer, Toledo, Ohio, Aug. 21; **Henry Ladner** (51), electrical engineer, Boonton, N. J., Sept. 10; **James L. Lake** (91), physicist, Raleigh, N. C., Sept. 1; **Robert K. Lamb** (48), of Cambridge, economist, Boston, Aug. 25; **William W. Leake** (68), surgeon, Fond du Lac, Wis., Aug. 26; **Max Lederer** (67), pathologist, Brooklyn, Sept. 13; **Moses D. Lederman** (83), ear, nose, and throat specialist, New York, Sept. 7; **Michael Levine** (66), of Yonkers, N. Y., biologist and cytologist, New York, Aug. 26; **David S. Likely** (71), internist, New York, Sept. 11; **Howard E. Lindeman** (69), of New York, gynecologist and obstetrician, Montauk Point, N. Y., Sept. 10; **James A. McDonnell** (64), aeronautical engineer, New York, Sept. 16; **William J. M. A. Maloney** (69), of New York, neurologist, Edinburgh, Scotland, Sept. 3; **Heyman R. Miller** (64), heart specialist, Poundridge, N. Y., Aug. 23; **Solomon Memat** (36), of Long Beach, L. I., podiatrist, New York, Sept. 14; **Ferdinand J. Neubauer** (66), astronomer, Monterey, Calif., Sept. 16; **Charles L. O'Neill** (68), surgeon, Newark, N. J., Aug. 26; **Leigh Page** (68), of New Haven, Conn., mathematical physicist, Randolph, N. H., Sept. 14; **E. Cooper Person, Jr.** (42), surgeon, New York, Sept. 5; **Albert Pike** (76), engineer and topographer, Tarboro, N. C., Sept. 3; **Joshua P. Pillsbury** (78), horticulturist and landscape architect, Elm City, N. C., Sept. 4.

Milton H. Redish (40), gastroenterologist and internist, New York, Aug. 29; **Erich H. Restin** (59), of Fort Pierce, Fla., surgeon, New York, Sept. 14; **Maurice G. Ricker** (83), explorer, educator, and photographer, Washington, D. C., Sept. 9; **Roy L. Robinson** (70), vice president, British Commonwealth Forestry Conference, Ottawa, Sept. 5; **Thomas K. Ross** (77), dentist, Fitchburg, Mass., Sept. 13; **Ole Salthe** (65), nutritionist, New York, Sept. 10; **Arthur J. Sandler** (—), of New York, electrical engineer, Rio de Janeiro, Aug. 31; **Emanuel B. Schoenbach** (40), bacteriologist and immunologist, Brooklyn, Sept. 6; **Robert C. Simpson** (73), naval architect, Groton, Conn., Aug. 19; **Harrison Smith** (71), civil engineer, Greenwich, Conn., Aug. 21; **Andres Gutierrez Solis** (52), traumatologist, Caracas, Venezuela, Aug. 22; **Alva B. Sowers** (68), oculist and ear specialist, Evanston, Ill., Aug. 31; **Eduard Strauss** (76), biochemist, New York, Aug. 24; **Freeman P. Stroup** (83), of Philadelphia, pharmaceutical chemist, Oil City, Pa., July 19; **Ernest K. Tanner** (75), surgeon, Cortland, N. Y., Aug. 30; **Franklin Thomas** (67), civil engineer, Pasadena, Aug. 27; **John E. Tress** (59), electrical engineer, Lansdowne, Pa., Sept. 13; **Adrian Van Muffling** (65), of New York, aeronautical engineer, New Milford, Conn., Sept. 7; **Ottomar H. Van Norden** (74), industrialist, New York, Aug. 28; **Gurth A. Whipple** (76), forester, Salamanca, N. Y., Sept. 11; **Harvey Whipple** (—), former secretary-treasurer, American Concrete Institute, Northville, Mich., Sept. 6; **William L. White** (44), of Arlington, botanist, Concord, Mass., July 31; **Frank N. Wilson** (61), internist, Stockbridge, Mich., Sept. 11.

Technical Papers

Early Devonian Deformation on Arbuckle Creek, Marion County, Kentucky

Willard Rouse Jillson

Frankfort, Kentucky

Significant faulting and folding of Richmond (Upper Ordovician) limestones and shales occur on the headwaters of Arbuckle Creek in central-southern Marion County at a point 7.3 airline miles southeast of Lebanon, Ky. The area of typical exposure is located about half a mile north of Muldraugh's Hill (1045′) and the Taylor County line in the central part of the commonwealth. Maximum local topographic relief is about 385′. This structural disturbance is unconformably overlain by beds of sandstone, sandstone conglomerate, and limestone of Onondaga and Hamilton (Middle Devonian) age, which exhibit neither the faulting nor the folding of the underlying Richmond sediments. Because of the comparative rarity of clear and well-defined mid-Paleozoic deformation in the eastern half of the Mississippi Valley, it has seemed important to outline the principal features of this accessible and most interesting occurrence.

The faults in this area on Upper Arbuckle Creek (660′–685′) were discovered by the writer on March 20, 1952, and have since been carefully studied and mapped. Undescribed previously in the literature, they are of the normal type, nearly parallel in extent and *en echelon* in pattern. They exhibit angles of

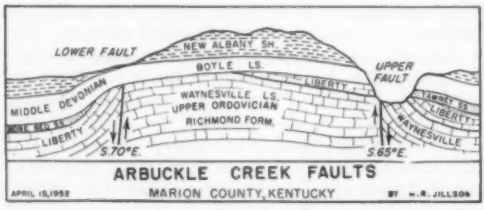

FIG. 1.

strike of S 70° E in the north break, and S 65° E in the south. Between these faults (Fig. 1) there exists a horst, or competent, rectilinear earth block, the width of which ranges from about 350′ to 400′. As exposed, this horst is made up of the lower part of the Liberty (uppermost division of the Richmond in this area) and the underlying Waynesville. The Liberty is identified by a long list of characteristic invertebrate fossils, chiefly brachiopods and bryozoans. The Waynesville, although carefully searched, appears to be essentially nonfossiliferous in this area.

The northern fault on Arbuckle Creek exhibits a downthrow of about 40′ or 50′ on the northeast side, with upturned limestone beds of the Liberty (including the *Columnaria alveolata* reef) dipping N 20° E at angles of 30°–45° downstream. These deformed beds offset the stratigraphically lower, grayish-green, compact, thin limy shales of the Waynesville, which dip 2°–3° N 30° E in the channel of the creek. The drag zone of actual movement is covered by small limestone and chert rubble in the bed of the creek. The abutting property is owned by Sam B. Luckett on the west and by John Spalding on the east.

The southern fault, exposed about 1500′ farther up the left fork of Arbuckle Creek, facing the property of Clem Tungate on the southwest, is of opposite pattern, but otherwise similar. Downthrow is on the southwest side, and the displacement is probably not more than 15′ or 20′. Here nicely exposed, almost longitudinally with the creek, upturned Waynesville limy shales on the downthrow side dip S 25° W from 30° to 50°, and are overlain at lesser angles by a thin, lower portion of the Liberty, which also contains the *Columnaria alveolata* horizon. This southern fault can also be plainly seen just below and on the Kirtland Branch of the right fork of Arbuckle Creek, ¾–1 mile to the northwest. The full extent of these faults is unknown, as they pass more distantly to the northwest and the southeast beneath undisturbed Middle Devonian sediments and are seen no more.

Both the northeast and the southwest downthrow blocks of these Arbuckle Creek faults are overlain by a tawny-colored, conglomeratic sandstone, which here exhibits a large amount of broken fishbones, plates, and very small teeth, together with numerous black to rust-colored phosphatic and ferrugenous nodules, ranging usually from 1 to 3 cm in diameter. Some, if not all, of these nodules may have originally been coprolites. Less commonly, an elongate, gray (apparently Richmond) limestone shore pebble, ranging from 6 to 9 cm in length and 3 to 6.5 cm in width, appears in this unusual clastic sediment, the dark-yellow color of which is, in many specimens, heightened into a distinct reddish brown by the rapid increase of fine bony material. This sandstone, which is usually tough and hard, is, however, frequently soft and friable at points close to the outcrop. It is composed in large part of clear, granular silica, generally of large grain-size, with a small but distinctly recognizable lime cement, which is unevenly distributed and may have been deposited by percolating ground or marine water during the late Paleozoic. An exceptionally interesting horizon, it is regarded as sufficiently distinctive and unusual to deserve specific stratigraphic recognition, and accordingly is here named the Bone Bed Sandstone. Close examination has revealed in this clastic horizon three fragmentary brachiopods, of as yet undetermined species but decidely Middle Devonian in appearance.

A very remarkable sedimentary unit, of probably

rather limited extent, the Bone Bed Sandstone has a thickness ranging from 1′ to 20′ in this particular area on Arbuckle Creek, 2′–4′ being common in close proximity to the faults, against which it thins and disappears. In the local stratigraphic section it is sometimes replaced by 1 or 2 in. of a tough, dark, sandy lime, which appears to be what A. F. Foerste, in 1906, working 30–50 miles away on the east side of the Cincinnati Arch, styled "the Kiddville layer" of the Middle Devonian lime. In any event, throughout this disturbed area on upper Arbuckle Creek, some 8′–20′ of the Boyle limestone (Middle Devonian), which overlies the Bone Bed Sandstone, the thin superjacent Duffin lime, and the succeeding New Albany (Upper Devonian) black shale, here exhibiting eroded thicknesses ranging from 1′ to 30′, unconformably override the faults and folds in the Upper Ordovician sediments (no Silurian and no Lower Devonian being present) and clearly define this structural disturbance as confined to the latter part of the early Devonian. The clarity of the angular unconformity, the faulted structure, and its unquestionable geologic dating as late early Devonian make this disturbance on Upper Arbuckle Creek (right and left forks) an ideal locality for field study.

Manuscript received May 29, 1952.

Isolation in Suckling Mice of a Virus from C_3H Mice Harboring Bittner Milk Agent[1]

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A virus, provisionally referred to as the K-virus, has been isolated by intracerebral inoculation of suckling mice from female C_3H mice carrying the Bittner milk agent. So far it has not been determined whether this virus is related to the tumor-inducing agent. It is felt, however, that such observations of the K-virus as have been made are of general interest and warrant publication. All mice used as a source of tissue for isolation, or attempted isolation, of virus were kindly provided by Howard B. Andervont.

Isolation was first accomplished in a litter of one-day-old regular Swiss mice inoculated intracerebrally with an extract of liver, spleen, and mammary adenocarcinoma of an adult C_3H mouse. Twelve days after inoculation, one mouse developed labored respiration and was found to have marked pulmonary consolidation. An extract of the lungs was passed intracerebrally to a second litter of Swiss mice. Succeeding passages were all brain-to-brain transfers. Virulence increased so that by the fifth passage nearly all mice inoculated became ill, usually in 8–10 days, with death following within 24 hr. Moribund mice were well nourished and had stomachs full of milk. Although all mice becoming ill on intracerebral inoculation developed labored respiration, only about 50% had gross evidence of pulmonary consolidation. So far, 13 consecutive passages have been made in suckling mice. Repeated cultures of brains harvested gave no evidence that bacterial contamination was a factor. Many thousands of suckling mice of the same stock have been inoculated intracerebrally in the course of experiments with other viruses without evidence of subsequent pulmonary consolidation, suggesting that the virus was contained in the original inoculum.

The K-virus will pass through a Selas .03 bacteria-tight filter, is resistant to freezing and thawing, will withstand 16 days' exposure to room temperature, and is unaffected by penicillin and streptomycin. By intracerebral inoculation, the virus has a titer of 10^{-8} and a somewhat lower titer by the intraperitoneal route. Subcutaneous inoculation has succeeded only with low dilutions. Pulmonary consolidation, occasionally with pleural fluid, has been produced by all routes. Intranasal inoculation has not shortened the incubation period. As mice becoming ill following inoculation with K-virus show no clinical or pathologic signs of CNS involvement, it is possible that success of brain-to-brain transfers rests primarily on blood contained in organ extracts. Continuing studies indicate that heart blood, when injected alone, is infectious. Young sucklings of all strains of mice so far tried have been found susceptible, including C_3H, C57 Black, A-strain, C-strain, and regular Swiss. Older mice, regardless of strain or route of inoculation, have been found resistant to obvious pathogenic effects of K-virus. Likewise, attempts to infect embryonated eggs, suckling rabbits, either suckling or adult hamsters, adult guinea pigs, meadow mice (*Microtus*), or deer mice (*Peromyscus*) have been unsuccessful.

A second probable isolation was made from the mammary glands of 2 lactating C_3H mice harvested 2 weeks after birth of the young. On first passage in C-strain mice, inoculated both intracerebrally and intraperitoneally at 2 days of age, 2 mice developed labored respiration after an incubation period of 9 days, one having characteristic pulmonary consolidation. Continued passages will be needed to demonstrate more definitely the identity of this second isolation with the original K-virus. Isolation of K-virus from mice known to carry the Bittner agent has generally proved difficult, as many attempts have been unsuccessful. Repeated attempts, likewise without success, have been made to isolate K-virus from strains of mice known to be free of the agent, using extracts of liver, spleen, and mammary tissue.

There has been little indication of relationship between the K-virus and other known mouse viruses, failure to infect older suckling or adult mice being a striking peculiarity. Affected mice show none of the neurological or muscular signs characterizing illness that is due to Coxsackie or Newcastle viruses. Furthermore, NDV immune serum does not neutralize the

[1] A preliminary report.

K-virus. Attempts to produce a K-virus immune serum in rabbits, guinea pigs, monkeys, and hens have not been successful by preliminary methods so far tried. Repeated examinations with Machiavello and Giemsa stains have revealed no bodies suggesting infection with the psittacosis group of viruses. It is believed that the K-virus is possibly a new, hitherto undescribed, latent virus of mice. Efforts are continuing, however, to discover whether the K-virus is actually identical or related to any known pathogens. So far I have no evidence to prove or to disprove relationship to the Bittner milk agent. Experiments have been instituted in cooperation with Howard B. Andervont to determine whether the K-virus has the capacity to induce mammary tumors in susceptible mice.

Manuscript received June 12, 1952.

Histology and Histogenesis of *Drosophila* Tumors

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Numerous tumor-bearing stocks are known in *Drosophila*. These stocks have been used for studies of the influence of x-rays (*1*), nutrition (*2*), temperature (*3*), and mammalian sex hormones (*4*) on the penetrance of the genetic factors involved. There has been a strong tendency to homologize these tumors with the melanomas of vertebrates (*5–7*).

Although Russell (*8*) contends that it is impossible to say from what type of tissue the tumors arise, it has so far been generally accepted that Drosophila tumors consist of imaginal cells showing atypical growth.

In a study of the histogenesis of the tumors of the *tu(2)49k* stock, the present author has prepared sections of larvae at ages from 47 to 100 hr after hatching, with age differences of 5 hr or less. The tumors of this stock become visible macroscopically at around 96 hr age.

The main features of the histogenesis are as follows: (1) No evidence of mitotic or amitotic cell divisions has been found in the tumorous tissues. (2) The blood cells constitute the sole element engaged in tumor formation. (3) Melanization of the larger blood cells starts before 47 hr age. A single lot of larvae 34 hr old show faint signs of this anomaly. (4) The brownish tinge in the anomalous cells of young larvae becomes progressively darker with age, obscuring the presence of a nucleus at around 75 hr. By 90–92 hr the cells appear black. (5) At around 70 hr, some of the smaller blood cells assume a spindle shape, and some of them become melanized as well. These cells are free in the hemocele. (6) From 78 hr on, aggregates of spindle-shaped cells may be found in the hemocele and in the caudal parts of the "blood-forming organ."

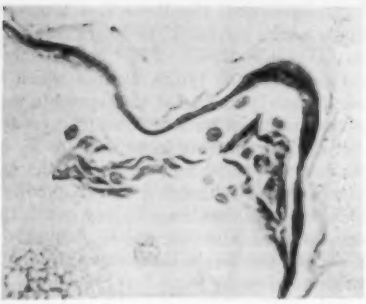

FIG. 1. Spindle-shaped, partly melanized blood cells, together with normal round ones, in the caudal hemocele of a 72-hr-old larva from *tu(2)49k* stock of *Drosophila melanogaster*.

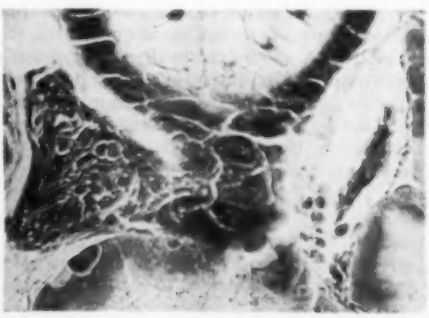

FIG. 2. Early tumor in the cardia region of a 92-hr-old larva from *tu(2)49k* stock. The tumor is not strongly melanized, and consists of spindle-shaped and round cells. Normal blood cells are seen around part of the tumor.

Fig. 1 shows free spindle-shaped blood cells in the caudal hemocele of a *tu(2)49k* larva, age 72 hr, together with normal round ones. Fig. 2 shows an early stage of tumor formation between the wall of the cardia and a gastric cecum, with an aggregate of partly melanized spindle-shaped cells surrounded by normal blood cells. This larva is 92 hr old.

After these results had been obtained in the study of *tu(2)49k* larvae, sections were prepared of larvae from five other tumor stocks. The ages of these larvae were not determined. The stocks used were *y 1(1)7, vg bw* mt^4, tu^g, *y* B^{263-43}, and *tu-36a*. The results of the examination of these sections may be summarized as follows: (1) All five stocks show melanized large blood cells. (2) Free spindle-shaped cells may be seen in the hemocele of larvae from tu^g and from *y* B^{263-43}. In the other three stocks, spindle-shaped elements are found only in the tumors themselves. (3) In tu^g stock the fat body seems to be attacked by the spindle-shaped cells at a comparatively early stage, and in *y* B^{263-43} there is some indication that early tumors are formed near the hind-gut. With the possible exception of tu^g, tumors free in the hemocele appear to be the most common type. (4) In no stock has there been found any indication of involvement of imaginal cells.

It will be seen from the above observations that, although the main principles of tumor formation appear to be common to all stocks, characteristic minor differences are still present between the several stocks. A number of problems present themselves in this connection, and further studies are in progress. A detailed report will be published elsewhere.

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Manuscript received April 21, 1952.

A New Plant Growth Regulator—α-Cyano-β-(2,4-Dichlorophenyl) Acrylic Acid

W. B. Ligett, Calvin N. Wolf, R. E. Hay, and D. P. Uhl

Research Laboratories, Ethyl Corporation, Detroit, Michigan, and Battelle Memorial Institute, Columbus, Ohio

In the course of a search for novel plant growth regulators, a new chemical compound, α-cyano-β-(2,4-dichlorophenyl) acrylic acid (Ethyl-214) was synthesized and tested in greenhouse experiments on tomato and marigold plants. When applied at low concentrations, this compound produced the striking effects of inhibiting the growth of tomato and the flowering of marigold.

The discovery of the growth inhibitory action of maleic hydrazide (*1*) has drawn attention to the possibilities of plant growth control without visible injury. Preliminary studies indicate that the inhibitory effect of α-cyano-β-(2,4-dichlorophenyl) acrylic acid on tomato is similar to that of maleic hydrazide. Both materials inhibit the growth of tomato without apparent injury. However, tomato plants treated with α-cyano-β-(2,4-dichlorophenyl) acrylic acid show a decrease in apical dominance, permitting activation of the axillary buds, whereas response to maleic hydrazide is an over-all slowdown of growth. The application of α-cyano-β-(2,4-dichlorophenyl) acrylic acid to budding marigold plants caused a marked delay in flowering. However, maleic hydrazide was ineffective at comparative concentrations in delaying the flowering of marigold. Thus, it appears that the new compound has a mode of action different from that of maleic hydrazide, and a different range of selectivity as a plant growth regulator.

α-Cyano-β-(2,4-dichlorophenyl) acrylic acid was synthesized by the condensation of 2,4-dichlorobenzaldehyde with cyanoacetic acid. After recrystallization from benzene, it is obtained as white leaflets, melting at 197.5°–198.3° C. The diethanolamine salt is obtained in the form of white crystals, melting at 137.9°–138.9° C. Further details of the synthesis of α-cyano-β-(2,4-dichlorophenyl) acrylic acid and its derivatives will be published elsewhere.

Preliminary toxicological data[1] have been obtained, employing a small number of animals. The approximate lethal dose of α-cyano-β-(2,4-dichlorophenyl) acrylic acid for rats, when given by oral administration, lies between 50 and 250 mg/kg body weight, and that of its diethanolamine salt lies between 250 and 500 mg/kg. Both the free acid and the diethanolamine salt have been applied to the abraded skin of rabbits. In each instance the rabbit survived a 24-hr period of contact with 250 mg/kg of body weight.

Four tests were used to evaluate the effects of α-cyano-β-(2,4-dichlorophenyl) acrylic acid on tomato plants: seed germination, lanolin paste, single leaf dip, and total spray. No evidence of unusual growth response was noted in the seed germination or lanolin

[1] Toxicity tests were conducted by J. F. Treon, of the Kettering Laboratory, University of Cincinnati.

FIG. 1. Effect of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, when applied to tomato plants at four different concentrations, 0.05, 0.1, 0.2, and 0.4% and control, 3 weeks following treatment.

paste tests. In the leaf dip and total spray tests, however, marked inhibition of growth resulted.

When a single leaf of young tomato seedlings was dipped in a 1% aqueous suspension of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, the treated leaf died, but no other immediate effects on the rest of the plant were noted. Ten days later, the treated plants were only one third the height of the control plants. At the end of a month, the height of the treated plants was one half that of the control.

Death of the plants resulted when a 1% suspension of the compound was sprayed on young tomatoes. However, when a 0.1% suspension was used, growth inhibition occurred without visible tissue damage. In the latter experiment 2-in. tomato plants, growing one to a pot, were sprayed with 10 ml of a 0.1% aqueous suspension of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, using 0.1% Tween 20 as the wetting agent. At the end of one week, the treated plants were noticeably smaller than the controls. Average measurements of height taken at the end of three weeks were: treated plants, 5.5 in.; control plants, 14 in. Although there was no tissue damage, and the color was normal, the treated plants exhibited formative effects, being unusually bushy with numerous axillary branches. The growth-inhibiting effect of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, when applied to tomato plants at four different concentrations, is illustrated in Fig. 1.

Preliminary studies have indicated that, on a mole basis, the diethanolamine salt of α-cyano-β-(2,4-dichlorophenyl) acrylic acid is more effective than the free acid in inhibiting growth of tomato. This increased activity is probably due to the greater water-solubility of the salt.

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Crystalline and Amorphous[1] Insulin-Zinc Compounds with Prolonged Action

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The presence of zinc in pancreas and in crystalline insulin has given rise to a series of investigations on the interaction between insulin and zinc. As a result, protamine-zinc-insulin has become extensively used. The clinical results have been rather disappointing, for the weak initial action of this preparation has been very troublesome, especially in cases of severe diabetes.

In an effort to develop more suitable insulin preparations for single injection, we have carried out some combined chemical, biological, and clinical experiments, designed to elucidate the interaction between insulin and zinc.

It was first discovered that phosphate ions, which are used in the protamine-zinc-insulin preparation, are able to influence the physical-chemical relation between insulin and zinc.

In Fig. 1, *A* illustrates the solubility of insulin as a function of pH in phosphate buffer (an acid solution of insulin—40 u/ml—is adjusted to different pH values, and the dissolved insulin is determined spectrophotometrically). It can be seen that all the insulin is dissolved at the pH of blood, 7.3, which presumably explains why isoelectrically precipitated insulin does not possess a sustained effect. *B* shows the solubility of insulin in the same buffer, to which has been added the same amount of zinc as is found in protamine-zinc-insulin—2 mg/1000 u. The conditions for solubility

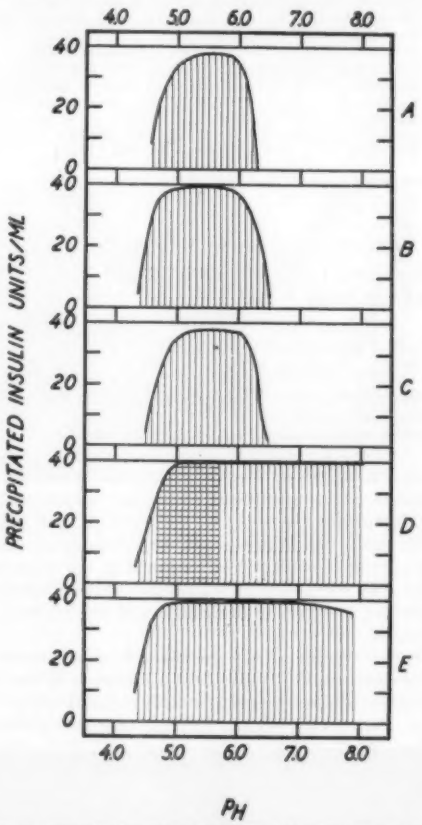

Fig. 1. Precipitation zone of insulin (40 u/ml) in: *A*, 0.01 mol sodium phosphate; *B*, 0.01 mol sodium phosphate with 2 mg zinc (as chloride)/1000 u; *C*, 0.01 mol sodium acetate: *D*, 0.01 mol sodium acetate with 2 mg zinc (as chloride) /1000 u; *E*, 0.01 mol sodium phosphate with 2 mg zinc (as chloride)/1000 u and 8.5 mg protamine/1000 u.

[1] Amorphous insulin, in this paper, refers only to the physical state of the insulin and not to the purity. The amorphous insulin is thus prepared by precipitation of dissolved crystalline insulin.

are altered only to a slight extent. *C* describes the solubility of insulin in acetate buffer. Only a slight deviation from the conditions in the phosphate buffer is seen, but on the addition of 2 mg zinc/1000 u there is a marked extension of the precipitation zone of the insulin, as shown in *D*. This and other experiments have established the fact that zinc has a great influence on the solubility of insulin as a function of pH in pure water, in acetate buffer, and in some other buffer solutions. The insulin is insoluble to the same degree as a zinc-protamine-insulin combination, as illustrated in *E*. Protamine (or other similar basic substances) is thus not a necessary factor for obtaining insolubility at the pH of blood. By using a small amount of zinc, as in protamine-zinc-insulin, insulin attains just as high or a higher degree of insolubility as in combination with protamine. The undissolved insulin contains chemically combined zinc. Phosphate buffer should not be used if this zinc effect is to be

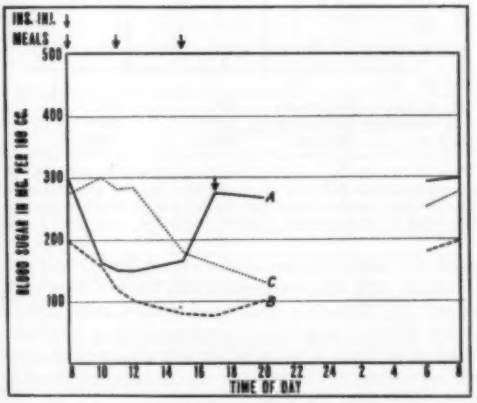

FIG. 2. Average blood-sugar curves (3–5 days) obtained with 3 depancreatized dogs. Average dose: 24 u. *A*, insulin-zinc (pH 2.7, 2 mg zinc/1000 u, solution. (Supplementary dose given at 5:00 P.M. when necessary.) *B*, amorphous insulin-zinc suspension (pH 7.2, 2 mg zinc/1000 u). *C*, protamine-zinc-insulin (NOVO) (pH 7.2, 2 mg zinc/1000 u).

obtained. The same applies to citrate buffer. Presumably the affinity of zinc for these substances is greater than for insulin.

Insulin preparations with the pH of blood, containing all the insulin in undissolved form, can thus be prepared by avoiding the presence of substances such as phosphate, citrate, ammonia, etc., which have a particular affinity for zinc. Our biological experiments, carried out at the same time on depancreatized dogs, clearly demonstrated that neither an acid solution of zinc and insulin (pH 3, 2 mg zinc/1000 u) nor an acid solution of protamine-zinc-insulin (protamine-zinc-insulin also contains 2 mg zinc/1000 u) possessed a sustained effect. This induced us to investigate whether the precipitated insulin-zinc had a prolonged action.

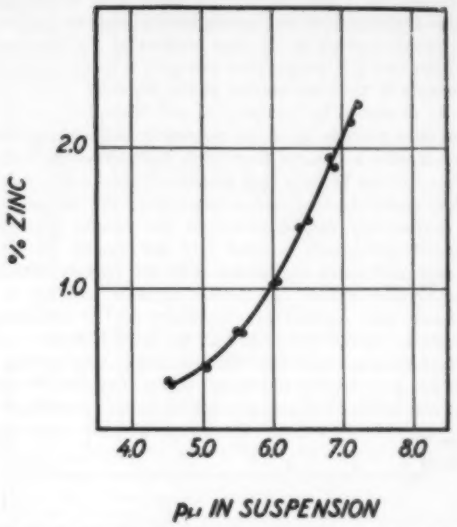

FIG. 3. Zinc content of insulin crystals (40 u/ml) suspended in 0.01 mol sodium-acetate with 2 mg zinc (as chloride)/1000 u as a function of pH.

The results clearly reveal a distinct prolonged effect of the undissolved insulin-zinc compound, as illustrated in Fig. 2, which shows a comparison between dissolved insulin and zinc (pH 3, 2 mg zinc/1000 u) and protamine-zinc-insulin (NOVO) (pH 7, 2 mg zinc/1000 u). The action of dissolved insulin and zinc ceases as early as 7–8 hr after injection, at which time both insulin-zinc and protamine-zinc-insulin exercise a pronounced effect. Fig. 1 *D* shows a squared area, which is the precipitation zone within which the amorphous insulin precipitate is completely or partly converted into a crystalline modification. Outside this zone the precipitate is stable and amorphous. The crystallization zone will vary somewhat with, for example, the amount of zinc, temperature, and time. Insulin crystals suspended in a solution of a zinc salt are preserved intact and completely undissolved in the pH range from 5 to 8, provided that substances which may interact with the zinc are not present. Other experiments have shown that the insolubility of amorphous and crystalline insulin caused by the presence of zinc demands an amount of zinc not less than approximately 0.5 mg zinc/1000 u.

Amorphous insulin and insulin crystals suspended in such zinc-containing media show, on analysis, a zinc content which is dependent both on the concentration of insulin and zinc used and on the pH value of the suspension. The relation between pH of suspension and the zinc content in the suspended insulin crystals is shown by the curve in Fig. 3. Insulin crystals, 40 u/ml, were suspended in solutions of various pH's, containing 2 mg zinc/1000 u and 0.01 mol sodium acetate. The increased zinc content of the crystals is not due to a simple precipitation of zinc hy-

droxide, as it also appears in a pH zone where the zinc hydroxide is not precipitated, just as a pronounced increase in the zinc content of the medium, within this pH range, does not give a corresponding increase in the zinc content of the crystals.

As described by Eisenbrand and Wegel (*1*), it has not been possible up to the present to prepare crystalline insulin with more than 0.8% zinc. However, from Fig. 3 it can be seen that insulin crystals under suitable conditions may contain more than 2% zinc.

Apparently the structure of the insulin crystals permits substances to enter into the crystals by diffusion and react chemically with the insulin within the crystal lattice. The insulin crystals with an increased zinc content are, contrary to the ordinary crystals, insoluble in water at the neutral point and retain their excessive zinc content, but if they are suspended in a neutral phosphate buffer they dissolve as the zinc is liberated and precipitate as zinc phosphate.

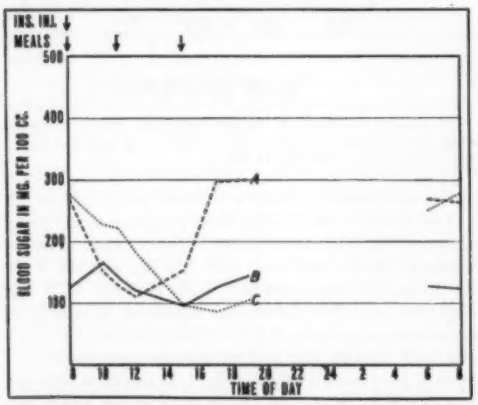

FIG. 4. Average blood-sugar curves (3–5 days) obtained with 5 depancreatized dogs. Average dose: 28 u. *A*, crystalline insulin NOVO, pH 2.7, solution; *B*, crystalline insulin-zinc suspension (pH 7.2, 1 mg zinc/1000 u); *C*, protamine-zinc-insulin NOVO (pH 7.2, 2 mg zinc/1000 u).

By increasing the zinc content of the crystals, not only the chemical but also the biological properties are altered. The action of ordinary insulin crystals suspended in water is not significantly different from that of ordinary dissolved insulin, as shown by Scott and Fisher, but in dog experiments with crystals of increased zinc content we found a striking prolongation of the insulin action.

Fig. 4 shows a comparison, on 5 depancreatized dogs, between (*A*) ordinary insulin (pH 3, 0.5 mg zinc/1000 u); (*B*) a suspension of insulin crystals with increased zinc content (pH 7, 1 mg zinc/1000 · u) —crystal size about 0.03 mm; and (*C*) protamine-zinc-insulin (pH 7, 2 mg zinc/1000 u). It appears that a suspension of these crystals possesses a markedly prolonged action, ensuring a low fasting blood sugar.

Up to the present, the action of the preparations containing amorphous or crystalline insulin-zinc and combinations of such preparations have been investi-

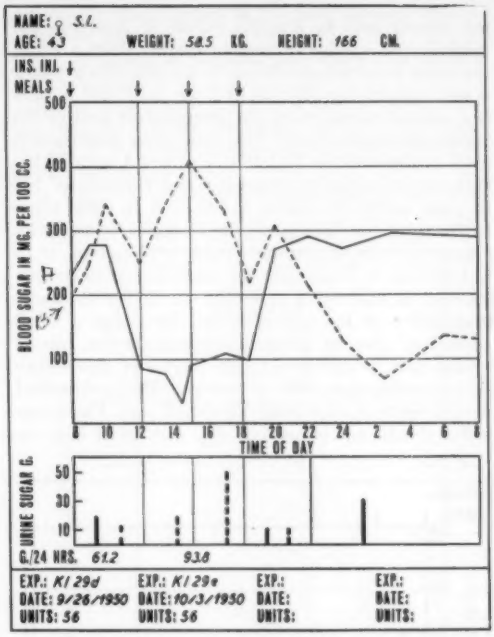

FIG. 5. Blood-sugar curves obtained with a diabetic, B. S. experimental method (*2*): *A*, crystalline insulin suspended in 0.9% sodium chloride solution, pH 6.0; *B*, crystalline insulin suspended in 0.9 sodium chloride solution, pH 6.0, 2 mg zinc/1000 u.

gated on a large number of diabetics.[2] The animal experiments were fully confirmed, and the chemical conditions for obtaining prolonged action were determined. With no exception a prolonged effect has been found in any preparation which contains, or will contain by adjusting the pH, all the undissolved insulin bound to zinc at the neutral point.

Fig. 5 shows, using the "B. S. experimental method,"[3] a comparison between two insulin preparations of the following composition: (*A*) insulin crystals suspended in physiological saline, 40 u/ml, pH 6.0, and (*B*) insulin crystals suspended in physiological saline containing 2 mg zinc/1000 u, 40 units/ml, pH 6.0. The insulin crystals suspended in water do not show any perceptible prolongation of action, in accordance with Scott and Fisher's results. On the other hand, if the suspension contains a small amount of zinc, 2 mg/1000 u (the same amount as in protamine-zinc-insulin), a pronounced retardation of the effect is obtained. The retarding effect of the

[2] Clinical investigations were performed at the Hvidøre Hospital, under the supervision of the chief physician, M. Jersild, whom we thank for permission to present illustrative graphs.

[3] The experimental technique described by Hallas-Møller (*2*) as the B. S. experimental method is, in brief: Under standard conditions (bed, a standard diet, regular-insulin-"preday") and at suitable intervals, 24-hr tests. In these 24-hr tests, one uses successively the insulin preparations it is desired to compare, so that they are characterized by a 24-hr blood-sugar curve as well as by excreted quantities of sugar.

zinc is not changed by decreasing the pH from 7 to 6, in spite of the parallel decrease in the zinc content of the crystals (Fig. 3). This and other experiments show that it is not a necessary condition for obtaining a prolonged effect that the crystals should possess an increased zinc content before the injection.

Fig. 6 shows (B. S. method) a comparison between

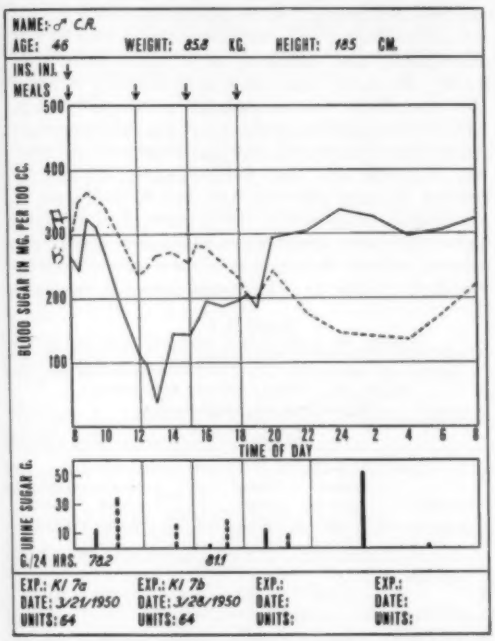

FIG. 6. Blood-sugar curves obtained with a diabetic, B. S. experimental method (2): *A*, crystalline insulin suspended in 0.01 mol acetate, pH 6.0, 2 mg zinc/1000 u; *B*, crystalline insulin suspended in 0.01 mol phosphate, pH 6.0, 2 mg zinc/1000 u.

(*A*) insulin crystals suspended in 0.01 mol sodium acetate buffer containing 2 mg zinc/1000 u, 40 u/ml, pH 6.0, and (*B*) insulin crystals suspended in 0.01 mol sodium phosphate buffer containing 2 mg zinc/1000 u, 40 u/ml, pH 6.0. The pH is 6.0, as the insulin crystals in phosphate-containing medium are dissolved at the neutral point (Fig. 1 B).

It appears from these experiments that the addition of phosphate in contrast to the addition of acetate completely neutralizes the protracted effect of an insulin crystal suspension containing zinc.

Fig. 7 shows single curves from 9 diabetics after injection of an insulin crystal suspension containing 2 mg zinc/1000 u (pH 7) and with a crystal size of about 0.01 mm. These curves clearly demonstrate the large range of activity of such a preparation.

The size of the insulin crystals used in the experiments (Figs. 4 and 7) is approximately 0.030 and 0.010 mm, respectively. Biological experiments point to the fact that preparations from crystals that are appreciably greater (0.075–0.1 mm) have a somewhat

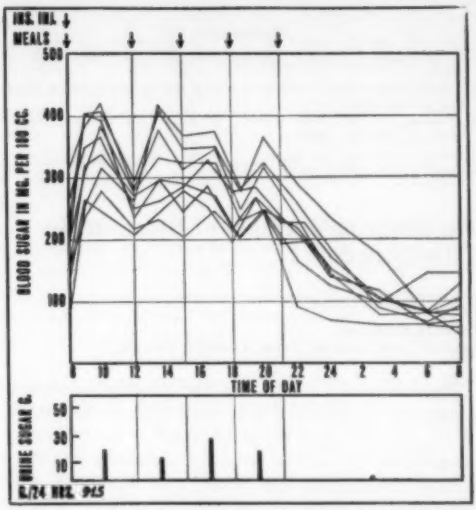

FIG. 7. Blood-sugar curves obtained from 9 diabetics; B. S. experimental method (2). Av dose: 55 u crystalline insulin-zinc suspension, pH 7.2, 2 mg zinc/1000 u.

more protracted action, just as, conversely, one obtains a somewhat faster action by grinding the crystals.

The following factors for the composition of the insulin-zinc preparations are essential for the biological effect: (1) The physical state of the insulin—amorphous, crystalline, large or small crystals; (2) the zinc concentration; and (3) the buffer. Owing to the fact that the insulin-zinc preparations are only based on the pure crystalline insulin and traces of zinc, they have so far never caused any allergic reactions.

The biological experiments here described are considered as preliminary steps in our efforts to develop insulin preparations with more suitable timing—i.e., a suitable adequacy between the initial and the retarded effect.

It is interesting to note that the retarding effect of zinc is exerted not only on insulin precipitated by protamine, globin, surfen, etc., but also on pure insulin alone which is made insoluble by combination with zinc. This is in agreement with, and supplements the findings of Scott and Fisher (*3*), who stated that the action of insulin precipitated by protamine or spermin was only significantly modified in the presence of small amounts of zinc. Other experiments, not reported here, have shown that other metals—e.g., the "crystallization metals," cadmium, cobalt, or nickel—can replace zinc. It is not yet possible to present the most suitable composition of the insulin-zinc preparations, as more clinical work is necessary.

In view of the fact that the organism, and especially the pancreas, contain zinc, the great influence of zinc on the insulin action may perhaps induce one to think of an *in vivo* relation between the two substances.

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The Reducing Potential of Illuminated Chloroplasts[1]

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The apparent limitation of the photolytic reaction to oxidants of standard potentials higher[2] than 0.0 v (*1, 2*), has prompted the publication of the following observations (*3*) on the reducing potentials that illuminated chloroplasts can attain. The redox potential that chloroplasts will finally establish with an oxidant in light is a reflection of the photoreducing intensity of the photolytic system. This potential was found to approach strongly reducing levels in washed chloroplasts freshly isolated, by the usual method (*4*), from leaves of Swiss chard. The isolated chloroplasts were suspended in distilled water and stored at 1° C.

In one type of experiment the final degree of reduction of methylene blue (MeBl) (at 10^{-5} *M*) by chloroplasts (at 3×10^{-6} *M* chlorophyll) was determined *in vacuo* photometrically, at pH 6.5, 15° C, and 1800 ft-c, a number of times over a period of several hours. The normal potentials (E_h) were then computed from the final percentages reduction of the dye, using the standard potential of 0.06 v for MeBl under the experimental conditions. The following positive, normal potentials were thus obtained from one series of determinations: at 1.5 hr after preparation of chloroplasts, 0.021 v; at 3.5 hr, 0.059 v; at 4 hr, 0.063 v; at 4.5 hr, 0.062 v; at 6.5 hr, 0.075 v; and at 9 hr, 0.078 v. The familiar kind of curve for loss of photolytic activity (*5*) was thus obtained. Extrapolation of such data shows that at the time of their isolation (zero time) the chloroplasts must be capable of a reducing potential in the negative voltage range.

In other experiments the potentiometric method (to be described elsewhere) was used to determine the course of reduction of several different oxidants by illuminated chloroplasts. The oxidants tested were 2,6-dichlorophenol indophenol, *o*-cresol indophenol, 1 naphthol-2-sulfonate indophenol, toluylene blue, thionine, cresyl blue, methylene blue, indigo tetrasulfonate, and indigo disulfonate, in order of decreasing standard potential. Whereas in air the rate and amount of drop of potential were directly related to the standard potential of the oxidant, in rough agreement with Aronoff's data (*6*), no regular relationships were found in the absence of oxygen. Thus the reoxidation of the added oxidant can obscure the redox state of the chloroplastic reductant. The following data were obtained with anaerobic (nitrogen) reaction mixtures containing 0.05 *M* phosphate buffer at pH 6.5, chloroplasts at a concentration of $5\text{–}10 \times 10^{-6}$ *M* chlorophyll, and oxidants at a concentration of 5×10^{-6} *M*, at 15° C and at a light intensity of about 1000 ft-c. MeBl was reduced the most rapidly—e.g., 1.14 *M*/min/*M* chlorophyll—yet it was not completely reduced. In comparison, 2,6-dichlorophenol indophenol, toluylene blue, and indigo tetrasulfonate were reduced at rates of 0.53, 0.53 and 0.02 *M*/min/*M* chlorophyll, respectively. Also, some dyes of both higher and lower standard potentials than MeBl were reduced by fresh chloroplasts to lower potentials than was MeBl (Table 1). The lowest potential measured was approximately −0.25 v (E_h), and it was achieved with toluylene blue. There is no reason to believe that this is close to the maximum reducing power of chloroplasts *in vitro*, but this value is probably the nearest of the above to the latter. The possibility of an electrode being poisoned was lessened by agreements between two electrodes per reaction mixture, and by reproducible results. The loss of photolytic activity sustained by the chloroplasts in each reaction mixture, during the course of these experiments, was not determined. However, the various oxidants in a given series of experiments (Table 1) were photolytically reduced by the same preparation of chloroplasts in separate vessels, simultaneously.

TABLE 1

Computed Standard Potentials (E_o') (Volt) of a Series of Oxidants and Their Normal Potentials (E_h) (Volt) before and after Reduction by Illuminated Chloroplasts

Oxidant	2,6-Dichlorophenol indophenol	Toluylene blue	Cresyl blue	Methylene blue	Indigo disulfonate
E_o' pH 6.5 15° C	0.283	0.169	0.116	0.060	−0.067
Initial E_h	0.435	0.448	0.496	0.471	0.470
E_h after 2.75 hr	0.071	−0.239	−0.046	0.011	−0.009
Potential drop (volt)	0.364	0.687	0.542	0.460	0.479

It can be concluded that characteristics of the oxidant, other than those associated with its standard potential, affect the apparent reducing activity of illuminated chloroplasts. The fact that photosynthesis occurs in the presence of oxygen and other oxidants of higher potential than CO_2 (*4*) may be another

[1] This work was conducted during part of the tenure of a predoctoral research fellowship of the Carnegie Institution of Washington at its Department of Plant Biology at Stanford, under C. S. French, to whom the writer is deeply grateful.

[2] The terminology is used by which the potential of the oxygen electrode is positive in sign.

example. In the light of the above results it appears less improbable that photosynthetic oxidants, of standard potentials lower than 0.0 v, may be quite strongly reduced by illuminated, freshly isolated chloroplasts in the absence of oxygen. Better methods of isolation (*7*) and of storage (*5*) of chloroplasts should help to establish such a postulate. A specific oxidant of low potential, the reduced form of which is not autoxidizable, may not require the absence of oxygen for its strong reduction.

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Observations on the Solubility of Some Cortical Hormones

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Several reports (*1, 2*) have indicated a difference in the clinical response of patients with arthritis to cortisone and hydrocortisone given by intra-articular or intramuscular injection as a saline suspension. In this connection, it became of interest to determine the solubility of these compounds in various biological fluids. The following report presents the results of solubility determinations of several crystalline derivatives of cortical hormones in distilled water, normal human plasma, a solution of human serum albumin, and human synovial fluid.

The normal human plasma was a commercially available, freeze-dried, irradiated product. It was restored to its original volume at time of use by the addition of sterile, pyrogen-free 0.1% citric acid solution. The normal human serum albumin was a salt-poor, concentrated solution containing 25 g of human serum albumin/100 ml.[1] The synovial fluid was obtained from arthritic joints of patients prior to intra-articular administration of steroid suspensions.[2]

A saturated solution was prepared by shaking an excess of the crystalline solid with 10 ml of test fluid in a centrifuge tube at 25° C for 1 hr. The clear solution obtained after centrifugation and filtration was used for analysis. The concentrations of dissolved material were determined by ultraviolet spectrophotometry or by the colorimetric method of Mader and Buck (*3*). Both methods were used in many of the determinations and showed good agreement.

A summary of the solubility data is given in Table 1. These data indicate that hydrocortisone acetate is much less soluble in the biological fluids tested than cortisone acetate, even though the solubilities in water are comparable. Both steroids are much more soluble in the unesterified form. No significant differences were apparent, however, in the solubility of the unesterified forms of cortisone and hydrocortisone in the fluids tested. The marked increase in solubility of cortisone tricarballylate in the biological fluids as compared with water undoubtedly is the result of salt formation. In sodium bicarbonate solution, the solubility of cortisone tricarballylate is in excess of 10 mg/ml at pH 7.5.

TABLE 1

SOLUBILITY OF CORTICAL HORMONES IN WATER AND BIOLOGICAL FLUIDS (mg/ml)

	Water	Human plasma	Human serum albumen	Human synovial fluid
Cortisone acetate	0.02	0.16	0.72	0.36
Cortisone (free alcohol)	.28	.75	1.28	.56
Hydrocortisone acetate	.01	.02	0.04	.04
Hydrocortisone (free alcohol)	.28	0.70	1.46	0.25
Cortisone tricarballylate (*4*)	.07	5.44	5.78	8.20
Cortisone propionate (*4*)	.008	0.14	*ca.* 0.1	0.09
Cortisone caprylate (*4*)	0 002	0.20	*ca.* 1.0	0.14

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[1] Supplied through the courtesy of the American National Red Cross.

[2] We are indebted to Joseph Hollander, of the University of Pennsylvania College of Medicine, for this material.

Comments and Communications

The Kirk Bryan Memorial Award

A GROUP of friends and professional colleagues of the late Kirk Bryan, of Harvard University, wishing to provide a fitting and enduring tribute to his accomplishments as teacher and scientist, have arranged for a Kirk Bryan Memorial Award, under the auspices of the Geological Society of America. It is hoped that this form of memorial will be representative of Professor Bryan's wide circle of friends in the different sciences, will signalize his achievements in coordinating the methods of geomorphology, geography, archaeology, soil science, and other fields in attacking common problems concerned with the Pleistocene, and will stimulate further research along the lines in which he pioneered.

The award will consist of two parts: an inscribed certificate and a cash stipend for the encouragement of research. The award is to be presented at the annual meetings of the Geological Society, at suitable intervals, to the author or authors of outstanding contributions in geomorphology or in the bordering fields in which Professor Bryan was particularly interested. The recipient of the award will be selected by a committee appointed by the Geological Society, and preference will be given to the younger men of the profession.

The award is to be based on the income from a Bryan Memorial Fund, set up within the Geological Society by contributions from Dr. Bryan's friends, former students, professional associates, and others who subscribe to the principle of the award. A three-year period is planned for the raising of sufficient funds to provide for an adequate cash stipend. It is understood that all contributions to the fund are deductible from taxable income. Contributions and pledges to the fund are now being solicited, and may be sent directly to the Geological Society of America, 419 W. 117th St., New York 27, specifically earmarked for the Bryan Memorial Fund. Other correspondence regarding the award may be addressed to the undersigned.

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Mortality and Regression of Sarcoma 180

THE Crocker Mouse Sarcoma 180 has been an excellent transplantable tumor for experimental studies for the past 37 years. Recently many small tumor screening laboratories have been set up to test compounds for antitumor activity. Some of the investigators who are new in the field of transplantable tumor work say that Sarcoma 180 has frequently regressed in their animal experiments.

During the past year, I have transplanted Sarcoma 180 into 5–10 mice at a time in order to study the regression and mortality rate. Table 1 gives a summary of the results obtained.

TABLE 1

MORTALITY AND REGRESSION OF SARCOMA 180

Death day	< 7	7–10	11–4	15–18	19–22	23–28	23–39	Total
Died	9*	16	35	30	41	9	5	145
Regressed	0	0	0	0	2	2	1	5

* These animals were infected or sick prior to being trocared.

The following suggestions are made to investigators who experience regressions with mouse Sarcoma 180:

1. The ideal weight of mice for therapeutic work is 18–22 g. Mice over 25 g in weight tend to have a slower rate of tumor growth.
2. Male mice over 5 weeks old from different cages should not be mixed, since adult males will always fight. This results in poor tumor growth, and at the same time the tumor can become contaminated from the bites of other mice.
3. Female mice are preferred, as they can be mixed with others from various cages without fighting. Pregnant females tend to have a poor tumor growth, and regressions are possible.
4. Tumor that is to be implanted should be cultured at the time of each passage. Contaminated tumors often regress.
5. Crystallized penicillin 1000 u/ml in saline solution prevents infection and also keeps the tumor moist. Streptomycin 0.01 g/ml may also be added if desired. Neither antibiotic inhibits tumor growth.
6. The larger the piece trocared, the larger the resulting tumor growth.

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Stable Nomenclature

THE demand for stability in nomenclature is a manifestation of the common yearning to maintain the *status quo*. Yet it is heard from scientists, who, of all people, should know that change is the universal rule. Mere opposition to change cannot long command respect, but is there any more valid reason for urging the stabilization of the technical names of organisms? Commonly, the underlying assumption is that if a name can be preserved in form its meaning will always be the same; but that is where hope has led judgment astray.

Taxonomy is a developing science; new characters significant in classification, are constantly being discovered; changes occur because of alteration in views as to what a genus or a species is; and, on the whole, the concepts of today are not those of 10 or 50 years ago, much less those of 200 years ago when the foundations of present-day nomenclature were being laid.

To illustrate: In 1913 W. W. Eggleston said of *Crataegus*, "About 300 species [recognized by him] . . . The genus has been of great taxonomic interest for ten years, about 1000 species having been de-

scribed, from the United States during that period." (In M. L. Britton and A. Brown, *Illustrated Flora Northern United States, Canada . . .*, 2nd ed., 294 [1913]). In 1935 L. H. Bailey noted that *Rubus* is "a most variable and perplexing genus, containing perhaps 400 fairly well-marked species and numberless intermediate forms. More than 3,000 species-names have been applied" (*Standard Cyclopedia of Horticulture*, 2nd ed., 3021 [1935]). And the same author, writing of *Rosa*, commented: "While some, as Bentham and Hooker, estimate the number [of species] at about 30, the French botanist Gandoger actually describes from Eu. and W. Asia alone 4,266 species" (*op. cit.*, 2981). Such splitting is not restricted to the genera mentioned; witness also *Iris*, *Viola*, and *Aster*, and it is not unknown in classification of the animal kingdom.

Contrast the figures cited with those for Linnaean species of those genera in 1753, which were: *Crataegus*, 9; *Rubus*, 10; and *Rosa*, 12. And consider what chance there is that a given name could have had the same content through subsequent time and all the upheavals indicated. The conclusion from this line of thought is that few, if any, names can have kept anything like the same meaning. Hence, so far as aiding in defining distribution, illustrating life history, or making any other practical use of the names is concerned, the literature would have no clearer significance than if the names had differed as often as the concepts shifted.

As names have not had the same meaning throughout their history, reliance upon a system of stable nomenclature compounds illusion. It is clear that the concepts embraced by the names may change with every revision, with every advance in taxonomic science. To have a really stable nomenclature would require a static classification—something that is both impossible and undesirable.

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On Scientific Reviewing and Writing

YOUR issue of April 18, 1952 on books is very welcome and, if I may follow the precept enunciated later, broadly sound; but there are other aspects to some of the issues raised, and these will repay discussion.

Scientific book criticism has two distinct functions that can, fortunately, be pursued simultaneously. First, the review should make clear whether the book is worth reading or buying. If the reviewer's name is well enough known in the subject, he need do little more than make a bald statement and then get on to writing about some related themes that interest him. Second, the review should discuss the subject, partly to show why the reviewer holds the views he does about the book, and partly because reading the book reviews should be a method of maintaining some acquaintance with sciences other than one's own. There is no advantage in pointing out errors in a good book; anyone capable of writing a good book will respond to a private letter in preparing a second edition. In a mediocre book it is generally worth while to explain what the deficiencies are; essentially, a mediocre book is one that would be good if it were modified a little. With a bad book errors need not be gone into in detail; the more outrageous, especially if comic, should be quoted, and that is all. The basic precept is that a review should leave the reader in no doubt whether the book is good, is marred by a few correctible defects, or stinks.

Dr. Bates suggests that reviewers should be younger, and that reviewing is a cheap, easy way to build up a library. I doubt it. However clear a review may be, its readers must take a great deal on trust, and the reputation of the reviewer matters. Furthermore, scientists not in permanent jobs naturally hesitate to be frank about a bad book by an author who is still influential. The unsigned review gets around this difficulty, but an unsigned critical review has little value unless it is very long. Expensive as books are, conscientious reading for review takes up an amount of time that, had it been spent coaching, examining, or even dishwashing, would bring in enough money for normal purchase. Thoughtful people do not review for economic motives; they have a variety of other motives—some of which may be less commendable.

The attempts of scientists to write popularly are rightly criticized by Frank Carey, but do journalists manage the business any better? Scientists use long and unusual words out of habit and thoughtlessness; journalists use them for effect. Each is wrong, but the error, as soon as it is realized, may be corrected. Slang is almost always a mistake, because it is ambiguous. A few lines back I used the word "stinks," but its ambiguity did not matter there, because all the possible meanings are suitably derogatory. But a light appearance should not be achieved at the expense of meaning, and in one or two places in his article Carey seems thus to have achieved it. The main contrast between the writing of a journalist and that of a good scientist seems to be that the former assumes only about a third of what he writes will be read. He therefore tends to use standard, easily recognized phrases instead of single words, and to repeat. The number of ideas contained in 1000 words is thus smaller than the number in a paper by a scientist. The scientist, on the other hand, tends to cover too much ground in an article and to put in too much detail. It would be better if scientists made their popular articles shorter, but the basic idea, that an article should be read rather than skimmed, is sound. If this were done, the digests would probably be put out of business, but this would not necessarily be a misfortune. The important thing is that working scientists should be encouraged to write for the general public. The effort educates the scientist, and the reader gets something different from his usual fare and something at least as good.

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A SERIOUS omission in Dr. Bates' article on "The Criticism of Scientific Books" (SCIENCE, **115**, 407 [1952]) is the important contribution of libraries to the publicizing of books.

Although approving Dr. Bates' suggestion that a journal such as SCIENCE should develop its book reviewing department to a greater extent, I feel that a better answer to the problem of keeping informed of new publications in science and other fields of knowledge is by continued use of the library. One visit by a general or specialized reader to a progressive public, university, or special library will convince him that libraries are no longer keepers of books, but rather promoters of books. Such a visit will very likely provide the book itself, many reviews of the book, and other material on the same subject.

I believe, also, that Dr. Bates is overly harsh in his opinion of the quality of book reviews. At least one exception to his statement that "all books on science get about the same treatment . . ." is the title *The Atom at Work*, by Jacob Sacks. This volume was selected by R. R. Hawkins, head, Science and Technology Department, New York Public Library, as one of the 100 essential technical books of 1950–51 (*Library J.*, **76**, 811 [1951]).

Nine reviews of this book were written by science librarians, scientists, and a science editor, as well as an unsigned review appearing in the *Saturday Review of Literature*. Certainly this is excellent coverage of a good book by a variety of qualified reviewers. Not one of the nine reviews mentioned "faulty documentation," "misprints," or "howlers." One review mentioned the index—not as "inadequate" but as "good."

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Book Reviews

King Solomon's Ring: New Light on Animal Ways. Konrad Z. Lorenz; trans. from the German by Marjorie Kerr Wilson. New York: Crowell, 1952. 202 pp. $3.50.

Only rarely does one encounter a book such as this. Konrad Lorenz is one of the world's outstanding naturalists, and here we have evidence that he is also an excellent narrator. Other men have learned to know certain species of animals as well as Lorenz knows his jackdaws, graylag geese, or ravens—you can find their reports in various technical journals—but the fact that Lorenz is a missionary of natural history sets him apart. He likes animals for what they are and he candidly states that this book is aimed at leading others to learn to like them.

With infinite patience, Lorenz has "kept" colonies of free-flying birds, an aquarium housing water shrews, and numerous other animals. His observations have been keen, and his descriptions comprehensive. He has successfully resisted the many temptations to anthropomorphize and yet he makes the reader aware of the mental and physical individuality of his subjects. After reading the chapter recording his 25 years with "The Perennial Retainers"—his jackdaws—you feel that you know them, as individuals and as a species.

There are times when Dr. Lorenz seems to generalize somewhat more than he should. His dismissal of the golden eagle as an "extremely stupid" creature, apparently on the basis of a single imperial eagle which he bought from a wandering menagerie, seems overly harsh. Certainly he demonstrates individual differences among other groups that he studied. These are but minor lapses, however.

In a way, this is a book of instruction. Dr. Lorenz lectures us, subtly, on morals, on pity, on laughter, all with animals as examples. His chapters on "Animals as a Nuisance," "Poor Fish," "Laughing at Animals," "Pitying Animals," and "Buying Animals" are all directed toward improving our relations with animals and, indirectly, with our fellow-men.

The title, based on the charming bit of folklore which supposed that Solomon talked to the animals, may result in some loss of readership, since it is rather abstruse. On the other hand, it may gain converts, since this is a book that, once picked up, is difficult to put down.

Julian Huxley's foreword is excellent, as might be expected. Marjorie Kerr Wilson's translation is smooth and unobtrusive. The illustrative sketches, which apparently are the author's, are both amusing and enlightening. I recommend the book to everyone.

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Miscellaneous Physical and Chemical Techniques of the Los Alamos Project: Experimental Techniques. Alvin C. Graves and Darol K. Froman, Eds. New York–London: McGraw-Hill, 1952. 323 pp. $4.00.

The third volume from Division 5 (Los Alamos) in the National Nuclear Energy series is a collection of miscellaneous physical and chemical techniques used in the early phases of the atomic energy project and originally collected as a laboratory manual for new personnel on the project. It was written by a group of 18 authors. The contents should be of especial interest to those working in nuclear physics with high energy machines: cyclotrons, van de Graaf generators, etc.

To give an idea of the scope of the book it is necessary to outline the contents of the six chapters. The

first chapter describes various methods of preparation of thin foils, especially uranium and plutonium, and also methods of making thin uniform foils of many other materials and compounds. The second discusses neutron sources, including natural sources (Ra-Be, etc.), and monoenergetic neutrons from charged particle reactions (essentially the same as the article in *Revs. Modern Phys.*, **21**, 635 [1949]). It includes the measurement and calibration of neutron sources and a detailed description of the construction of a BF_3 filled proportional counter. The third chapter gives the elementary theory of the betatron, a brief description of betatron construction and operating circuits, and a method of using the betatron for the production of isolated pulses of γ-rays. The fourth chapter discusses the modulation of cyclotron beams by arc modulation, and deflection modulation, the modulation of Cockroft-Walton and van de Graaf generators by deflection of the ion beam, and the use of these modulated beams in a slow neutron time-of-flight spectrometer. The fifth chapter contains descriptions of two diffusion pumps used in the project and of various types of vacuum seals and bushings. It also discusses the vacuum evaporation of metals. The sixth chapter covers optical methods and instruments, principally oscillograph cameras and high-speed cameras of various designs.

This short résumé can give only a general idea of the contents of the book. There are more than 160 figures. Many of these are detailed construction drawings, complete circuit diagrams, and graphs. The remainder are photographs, sketches, and block diagrams.

The book is clearly written, and the descriptions of the various techniques are quite complete, including sketches and detailed diagrams. Although some of the techniques are outdated, on the whole the book should make a valuable addition to the experimental physics library.

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Association Affairs

Revision of the AAAS Constitution and Bylaws

Howard A. Meyerhoff, *Administrative Secretary*

When the Association met at St. Louis in 1946, one of the important actions taken was the adoption of a new constitution (Science, **103**, 245 [1946]). It was recognized that the Association's bylaws should have been revised simultaneously so as to conform with the new constitution, but it was not until 1950 that any serious attempt was made to harmonize bylaws and constitution. At that time a committee comprising Kirtley F. Mather, *Chairman*, Clarence E. Davies, Karl Lark-Horovitz, Roger Adams, and Howard A. Meyerhoff, *Secretary*, turned to the task but soon concluded that the 1946 constitution required amendment or replacement. In many particulars it was so specific as to usurp the function of bylaws and, in prescribing certain administrative procedures, it was not only at variance with current practice but precluded the flexibility that is essential to the efficient conduct of business in an organization as large as the AAAS.

At Cleveland, on December 29, 1950, the Council authorized the committee to revise the constitution, in addition to preparing a new set of bylaws. The Council also approved in principle the basic changes that are embodied in the following document, in which constitutional articles and related bylaw provisions are printed consecutively. This document is merely a semi-final draft of a new constitution and bylaws, the final drafts of which, it is hoped, will be placed before the Council for action at meetings in St. Louis, December 27 and 30, 1952. Conferences with the Association's legal and financial advisers have indicated the need for some revision in Article II, Section 3, of the bylaws; in Article V, Section 2, of the bylaws; in Article XI, Section 1, of the constitution, and several sections in the corresponding article of the bylaws. Other modifications may be prompted by suggestions received from members, who are herewith invited to comment and to send any suggestions to the chairman of the committee or to the Administrative Secretary without delay.

In conformance with Article XI of the constitution now in force, the final drafts of the proposed constitution and bylaws will be published in Science and in The Scientific Monthly in November, at least one month prior to the annual meeting of the Association, and the Council will be asked to act upon the final drafts at one of its sessions, either on December 27 or December 30.

The most significant change contained in the proposed constitution is in the allocation of responsibilities. At present it is stipulated that "control of all affairs of the Association is vested in the Council, which shall have the power to review and to amend or rescind its own actions and all actions taken by the Executive Committee." It is obvious that the Council is not in a position to assume such responsibilities but must delegate them to carefully selected representatives of its own choosing; hence, in the new constitution it is proposed to give the Council the responsibility of electing the members of the Board of Di-

rectors (which will replace the present Executive Committee), and to this Board will be delegated the duty of managing the business affairs of the AAAS. Inasmuch as the members of the Board will be individually and collectively responsible to the Council, which also retains the power to determine and to define policies, the Council remains the governing and the controlling body, as it should; it merely relinquishes a role it cannot satisfactorily fill—namely, that of being an administrative body.

It is hoped that the members of the Association, as well as of the Council, will endorse this proposal, which will enable the administrative staff, under the direction of the Board of Directors, to carry on the ramified business functions more efficiently and with fewer legal involvements than can be achieved under the 1946 constitution. The draft of the proposed constitution and bylaws follows.

Constitution—*Article I*

Section 1. The American Association for the Advancement of Science was incorporated by an act of the General Court of the Commonwealth of Massachusetts in 1874. The Association is a nonprofit scientific and educational body.

Section 2. The objects of the American Association for the Advancement of Science are to further the work of scientists, to facilitate cooperation among them, to improve the effectiveness of science in the promotion of human welfare, and to increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

Bylaws—*Article I*

Section 1. The objects of the Association shall be accomplished by conducting meetings and conferences of those interested in various branches of science and education, producing and distributing publications, administering gifts and bequests as prescribed by the donors thereof, supporting research, making awards to recognize accomplishments in science, cooperating with other organizations in the advancement of science, and engaging in such other activities as shall have been authorized by the Board of Directors.

Constitution—*Article II*

Section 1. The membership of the Association shall consist of Members, Fellows, and Associates. Individuals in any of these three groups may become life members, emeritus members, and sustaining members in accordance with the provisions of Section 5 of this Article and with such relevant rules as the Board of Directors shall have prescribed.

Section 2. Members. Any person, institution, or organization may be admitted to the grade of Member. Each Member shall have such rights and privileges and shall pay such annual dues as the Board of Directors shall have prescribed.

Section 3. Fellows. Any person who shall have made a meritorious contribution to science may become a Fellow of the Association under such procedures as the Board of Directors shall have prescribed.

Section 4. Associates. Any person who shall have a record of leadership in any field related to science and who wishes to cooperate in the advancement of science may become an Associate of the Association under such procedures as the Board of Directors shall have prescribed.

Section 5. (*a*) *Life Members.* Any person making the Association a life-membership contribution of such amount as the Board of Directors shall have prescribed may be admitted to life membership. Each Life Member shall be exempt from the payment of annual dues and shall have all the privileges of an annual member throughout life.

(*b*) *Emeritus Members.* Any individual annual member may be admitted to emeritus membership under such conditions as the Board of Directors shall have prescribed. Each Emeritus Member shall be exempt from the payment of annual dues and shall have all the privileges of an annual member throughout life.

(*c*) *Sustaining Members.* Any person making to the Trust Funds of the Association a sustaining membership contribution of such amount as the Board of Directors shall have prescribed shall be the founder of a Sustaining Membership, which shall bear his name and shall be maintained in perpetuity as a trust. Each incumbent of a sustaining membership shall have all the privileges of a life member. The first incumbent of a sustaining membership may be either the founder himself or another person named by him, as he may choose. On the death or resignation of an incumbent, the Board of Directors shall name another person to hold the membership throughout life.

Bylaws—*Article II*

Section 1. Members who have paid dues for fifty years may be excused from further payments and still retain all the privileges of membership.

Section 2. Members may be elected by the Board of Directors to be Fellows of the Association and Fellows so elected shall remain Fellows only so long as they retain membership. If a Fellow discontinues his membership and subsequently rejoins the Association, he shall automatically again become a Fellow from the time of rejoining, without another election. Members are eligible to nomination for fellowship if they have contributed to the advancement of science either by the publication of original research or in other significant manner. Nominations for election to fellowship may be made by any three Fellows or by the administrative secretary or by the section committee in whose field the nominee's scientific work mainly lies.

Section 3. The Board of Directors may exclude from the Association anyone who has made improper use of his membership or whose membership is regarded as detrimental to the Association.

Constitution—*Article III*

Section 1. The officers of the Association shall be (*a*) general officers elected from among the Fellows by ballot of the Council, and (*b*) administrative officers elected by the Board of Directors as prescribed in Section 3 of this Article.

Section 2. General Officers. The general officers of the Association shall be a president-elect, a president, a retiring president, and a vice president for each section. The term of office of the president-elect and of the vice presidents shall begin on the January 15 following their election. At the close of the one-year term of the president-elect he shall become president, and at the close of the one-year term of the president he shall become retiring president. In the event of a vacancy in the office of the president, the president-elect shall become president. In

the event of a vacancy in the office of president-elect, the Board of Directors shall make a pro tempore appointment to hold until the vacancy shall have been filled by ballot of the Council. In the event of a vacancy in the office of vice president the Board of Directors shall fill the vacancy by appointment.

Section 3. Administrative Officers. The administrative officers shall be an administrative secretary, one or more associate or assistant secretaries, a treasurer, and, in addition, a secretary for each section. The administrative secretary, the associate or assistant secretaries, and the treasurer shall be elected by the Board of Directors. The secretaries of the sections shall be nominated from among the Fellows by the respective section committees and elected by the Board of Directors. The terms of office of each administrative officer shall be determined by the Board of Directors. The Board of Directors shall fill vacancies in the administrative offices.

Section 4. The duties of the officers shall be customary to those of the office and as further defined in the bylaws.

Bylaws—*Article III*

Section 1. The administrative secretary shall serve as secretary to the Council and to the Board of Directors; he shall be in charge of the Association's offices and shall manage the affairs of the Association in accord with procedures determined by the Board of Directors. He shall be an ex officio member of all standing committees.

Section 2. The treasurer shall perform the usual duties and those assigned in the bylaws.

Section 3. Reports of the administrative secretary and the treasurer shall be made in the manner prescribed by the Board of Directors.

Constitution—*Article IV*

Section 1. The Council shall perform duties prescribed in the constitution and shall act as an advisory body in matters pertaining to the general policies of the Association.

Section 2. The Council shall consist of (*a*) the president-elect, the president, retiring president, the vice presidents, secretaries of the sections, the administrative secretary, the treasurer, and the eight (8) elected members of the Board of Directors; (*b*) one Fellow elected by each regional division of the Association; and (*c*) the representatives of affiliated organizations as provided in Article VIII of this constitution. Each Council member shall serve until his successor shall have taken office. The president shall be chairman of the Council; if the president shall be unable to serve as chairman at any session, the Council members in attendance shall elect a chairman for that session. Twenty (20) members of the Council shall constitute a quorum for the transaction of business.

Section 3. The Council shall meet during the annual meeting of the Association and at other times on the call of the president or upon the written request of twenty (20) members of the Council.

Bylaws—*Article IV*

None.

Constitution—*Article V*

Section 1. The Board of Directors is the legal representative of the Association and as such shall have, hold, and administer all the property, funds, and affairs of the Association.

Section 2. The Board of Directors shall consist of eleven (11) members, the president-elect, the president, the retiring president, and eight (8) Fellows elected by the Council, two each year, for a term of four years. At any election of members of the Board of Directors not more than one Fellow serving his fourth consecutive year as an elected member may be re-elected. In the event of a vacancy in the office of an elected member of the Board of Directors, his successor for the remainder of the year shall be elected from among the Fellows by the Board of Directors and, for the remainder of the unexpired term, his successor shall be elected by the Council at the next annual election. Five (5) members of the Board of Directors shall constitute a quorum for the transaction of business. The retiring president of the Association shall be chairman of the Board of Directors. If he shall be unable to serve at any session of the Board, the Board members in attendance shall elect a chairman for that session. The administrative secretary and treasurer shall be ex officio members of the Board of Directors without vote.

Section 3. The Board of Directors shall hold four (4) meetings a year, one of which will be at the annual meeting. The Board of Directors shall also meet at the call of the chairman.

Section 4. The Board of Directors shall appoint such committees as may be necessary to aid in the management of the Association. The duties of standing committees shall be stated in the bylaws.

Section 5. The term of office of each of the eight (8) regularly elected members of the Board of Directors shall begin on January 15 following his election, and each shall serve until his successor shall have taken office.

Bylaws—*Article V*

Section 1. The committees shall be standing as provided in the bylaws or special as the Board of Directors approves.

Section 2. The Investment Committee shall advise the Board of Directors regarding purchase and sale of securities for the Association and shall make recommendations to the Board of Directors on financial questions. The Investment Committee shall consist of five (5) members appointed by the Board of Directors and selected from outside the Board of Directors, and the treasurer and administrative secretary. Each appointed member shall serve a term of five years, the term of one member expiring on January 15 of each year. Each shall serve until his successor shall have taken office.

Section 3. The Committee on Affiliation and Association shall review applications for affiliation or association with the Association and make recommendations thereon to the Board of Directors. The committee shall consist of five (5) members appointed by the Board of Directors. Each member shall serve a term of five (5) years, the term of one member to expire on January 15 of each year. Each shall serve until his successor shall have taken office.

Section 4. The Publications Committee shall give continuing scrutiny to the publications of the Association, the policies pertaining thereto, and make recommendations thereon to the Board of Directors. The committee shall consist of five (5) men appointed by the Board of Directors. Each member shall serve a term of five (5) years, the term of one member to expire on January 15 of each year. Each shall serve until his successor shall have taken office.

Constitution—*Article VI*

Section 1. The Association shall be organized in sections in accordance with the fields of interest of its members, as determined by the Council. Each member of the Association may designate the section in which he wishes to be enrolled and may designate an additional section in which he is interested.

Section 2. The vice president for a section shall be ex officio chairman of that section.

Section 3. The affairs of each section shall be managed by a section committee consisting of (*a*) the chairman and the secretary of the section; (*b*) other members of the Council who are primarily enrolled in the section; and (*c*) four (4) Fellows, one elected each year by the section committee for a term of four (4) years. No person shall serve concurrently on more than one section committee. If an elected member of a section committee shall have resigned or died, his successor for the remainder of the unexpired term shall be elected from among the Fellows by the Board of Directors, from nominations made by the section committee. One third of the members of a section committee shall constitute a quorum for the transaction of business.

Section 4. The section committee of each section shall promote the work of the Association in its own field and may organize subcommittees for that purpose. It shall arrange such section programs as it shall deem desirable for meetings of the Association, either separately or in cooperation with other sections of the Association or with independent societies. With the approval of the Board of Directors a section committee may arrange section meetings to be held at places and times other than those of Association meetings.

Bylaws—*Article VI*

Section 1. Council representatives of affiliated organizations which are not specifically related to an established section of the Association may be assigned to section committees in accordance with their requests.

Constitution—*Article VII*

Section 1. Regional divisions and local branches of the Association may be authorized by vote of the Council, for the purpose of promoting the work of the Association in their respective territories.

Section 2. Each regional division or local branch shall elect its officers for such terms as it shall prescribe and shall hold its meetings and conduct its affairs as it shall deem desirable, subject to the relevant provisions of this constitution and of the bylaws of the Association, and to such special provisions as the Board of Directors of the Association shall have established.

Bylaws—*Article VII*

Section 1. Regional divisions authorized by the Council have full control of their meetings, of their affiliations with other scientific organizations, and of all activities to promote the advancement of science in their territory.

Section 2. The Pacific Division (organized in 1915) includes members of the Association resident in British Columbia, Washington, Oregon, California, Idaho, Nevada, Utah, and the Hawaiian Islands.

Section 3. The Southwestern Division (organized in 1920) includes members of the Association resident in Arizona, New Mexico, Colorado, Sonora, Chihuahua, and Texas west of the 100th meridian.

Section 4. The Alaska Division (organized in 1951) includes members of the Association resident in Alaska.

Section 5. Each division shall receive for its expenses an annual allowance not to exceed one dollar for each of its members in good standing.

Constitution—*Article VIII*

Section 1. To facilitate cooperation between the Association and other organizations, and among the latter, the Council may, on recommendation of the Board of Directors, elect an organization to be an official affiliate.

Section 2. Each organization thus designated an affiliate shall be entitled to name one Fellow of the Association to represent it in the Council; if it has more than 100 members who are Fellows of the Association, it shall be entitled to name an additional Fellow to represent it on the Council.

Section 3. On recommendation of the Board of Directors, the Council may elect an organization to be an official associate. Associated organizations shall have the same rights and privileges as affiliated organizations except for representation on the Council.

Bylaws—*Article VIII*

Section 1. The names of affiliated and associated organizations shall be published from time to time as directed by the Board of Directors.

Section 2. Affiliated academies of science shall receive for research an annual allowance of fifty cents for each of their members who is also a member in good standing of the Association.

Constitution—*Article IX*

Section 1. The Association shall hold an annual meeting each year at such time and place as the Board of Directors shall have determined. Other meetings of the Association or of its sections may be authorized by the Board of Directors.

Bylaws—*Article IX*

Section 1. The programs and arrangements for the Association meetings shall be under the general direction of the Board of Directors.

Constitution—*Article X*

Section 1. The publications of the Association shall be issued in such manner as the Board of Directors may direct.

Bylaws—*Article X*

Section 1. The publications of the Association shall be (*a*) SCIENCE, (*b*) THE SCIENTIFIC MONTHLY, (*c*) *Proceedings*, and (*d*) such other special publications as the Board of Directors may direct.

Section 2. The Association shall not be responsible for statements or opinions advanced in papers or in discussions at meetings of the Association or its sections, divisions, or branches, or printed in its publications.

Section 3. The Association reserves the right to copyright, at the discretion of the Board of Directors, any of its papers, discussions, reports, or publications.

Constitution—*Article XI*

Section 1. The deposit, investment, and disbursement of all funds shall be subject to the direction of the Board of Directors.

Bylaws—*Article XI*

Section 1. All funds shall be paid into the business office of the administrative secretary, where they shall be entered in the books of the Association, and deposited to the account of the treasurer in a bank designated by the Board of Directors.

Section 2. All bills against members and others shall be made and collected by the business office of the administrative secretary.

Section 3. All expenditures shall be made in accordance with the budget of appropriations as adopted by the Board of Directors.

Section 4. All payments shall be made upon competent certification as to correctness and proper authorization by the business office from a Business Office Account kept in a bank designated by the Board of Directors.

Section 5. The treasurer shall reimburse the Business Office Account for payments made therefrom upon orders signed by the administrative secretary of the Association; or in the absence or temporary incapacity of the administrative secretary by an associate or assistant administrative secretary of the Association.

Section 6. Checks against the accounts of the Association will bear two signatures, from a list of individuals determined by the Board of Directors.

Section 7. The securities of the Association may be bought, sold, or exchanged only upon written order of two of the following: chairman of the Investment Committee, vice chairman of the Investment Committee, treasurer, and administrative secretary.

Section 8. The business office of the administrative secretary shall keep proper accounts of all financial transactions of the Association.

Section 9. The accounts of the Association shall be audited and approved annually by a chartered or other competent public accountant selected by the Board of Directors.

Section 10. The administrative secretary shall have the authority to enter into contracts for the Association, but contract authorizations must be within the budget authorizations made by the Board of Directors.

Section 11. The activities of the Gordon Research Conferences shall be administered according to procedures established by the Board of Directors.

Constitution—*Article XII*

Section 1. Amendments to this constitution shall be approved by the Board of Directors after publication in substance in SCIENCE and THE SCIENTIFIC MONTHLY at least one month prior to an annual meeting of the Association and ratified by a two-thirds vote of the Council members present in a Council session of that meeting. Ratified amendments shall be effective upon adoption and shall be published promptly in SCIENCE and THE SCIENTIFIC MONTHLY.

Bylaws—*Article XII*

The bylaws may be amended by majority vote of the Board of Directors, provided notification of the proposed amendment has been mailed to each member of the Board at least twenty (20) days prior to the meeting.

Corvallis Meeting of the Pacific Division

Robert C. Miller

California Academy of Sciences, San Francisco

THE Pacific Division of the AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE held its thirty-third annual meeting on the campus of Oregon State College at Corvallis, June 16–21, 1952. With 17 associated and affiliated societies participating in a program of some 430 scientific papers, and a registered attendance of 1095 persons, this was one of the largest meetings the division ever held.

In contrast to meetings in metropolitan areas, delegates were fed and housed at the college, and all activities and entertainment centered there, thus making for a compact, well-integrated meeting. The attractive surroundings, the excellent facilities of the college, the atmosphere of friendly hospitality, and the careful planning of the local committee combined to make this not only a successful but a memorable occasion.

Registration headquarters were in the Memorial Union building, which, in addition to housing the Faculty Club and the Student Bookstore, provides dining facilities and commodious, attractively furnished quarters for informal meeting and conversation. The reception to delegates by President and Mrs. A. L. Strand on Tuesday afternoon was held there, as was a social evening following the address on Wednesday by H. A. Spoehr, of the Carnegie Institution of Washington, Stanford University.

Dr. Spoehr, retiring president of the Pacific Division, gave an able and thought-provoking address on "Society in the Grip of Science." He was preceded on Tuesday evening by F. W. Went, of the California Institute of Technology, who spoke on "Climate and Plant Growth," and was followed on Thursday evening by Henry Eyring, of the University of Utah, who spoke on "Some Important Chemical Reactions in Agriculture and Forestry." These three evening lectures, together with the divisional symposium, a chemistry symposium on Friday afternoon, and the meeting of the Council of the division, constituted the only general sessions. The other sessions were given over to the meetings of the associated and affiliated societies.

The divisional symposium, on "Basic Research in Relation to Agriculture and Forestry," included the following papers: "Basic Research in the Improvement of Forestry," by F. I. Righter, California Forest and Range Experiment Station, Berkeley; "Contributions of Rumen Microbiology to Agriculture," by R. E. Hungate, State College of Washington, Pullman; "Electron Microscopy of Biological Objects Prepared by a New Freeze-drying Technique," by Robley Williams, University of California, Berkeley.

The meeting of the Council on Wednesday afternoon was addressed informally by Kirtley F. Mather, retiring president of the AAAS, and by Raymond L. Taylor, Assistant Administrative Secretary. At this meeting action was taken to amend the constitution, to

give recognition to the recently formed Alaska Division of the AAAS by detaching Alaska from the geographical area of the Pacific Division.

A. H. Sturtevant, of the California Institute of Technology, was named president-elect of the Pacific Division. President for the coming year is C. D. Shane, of the University of California, director of the Lick Observatory; H. A. Spoehr, the retiring president, becomes chairman of the Executive Committee. Phil E. Church, of the University of Washington, was elected a member of the Executive Committee. G. Ross Robertson, of the University of California at Los Angeles, and G. L. Pickard, of the University of British Columbia, Vancouver, were elected members-at-large of the Council.

In response to invitations pending, it was decided to hold the next meeting of the Pacific Division in Santa Barbara, June 15–20, 1953, and the 1954 meeting at the State College of Washington in June, the specific dates to be agreed on later.

The following societies participated in the Corvallis meeting with programs ranging from one to eight half-day sessions: American Chemical Society (Puget Sound, Richland, Washington-Idaho Border, and Oregon sections); American Meteorological Society (national meeting); American Nature Study Society (Western Division); American Phytopathological Society (Pacific Division); American Society for Horticultural Science (Western Section); American Society of Ichthyologists and Herpetologists (Western Division); American Society of Limnology and Oceanography (Pacific Section); American Society of Plant Physiologists (Western Section); Association of Pacific Coast Geographers; Botanical Society of America (Pacific Section); Cooper Ornithological Society; Ecological Society of America (Western Section); Herpetologists League; Pacific Northwest Bird and Mammal Society; Society of American Foresters (Columbia River Section); Society of Systematic Zoology (Western Section); and Western Society of Soil Science.

In addition to the usual society luncheons and dinners, there were special events for wives of delegates, recreational activities for children, tours of the campus, and field trips and excursions to points of interest in the surrounding country. A unique social function was an evening picnic for the entire group of delegates, held in Avery Park, a short distance from the campus. Several hundred persons gathered to eat Chinook salmon, barbecued Indian style on upright stakes around a large open fire. The pleasant spring evening, the smell of pine smoke mingled with the delicious aroma of outdoor cooking, and the opportunity for good fellowship and conversation provided an occasion not soon to be forgotten.

The college campus was a very busy place at the time of the divisional meetings. The regular summer session was under way, and a special summer session was also being held for some 2000 4-H Club boys and girls. The smoothness with which all these activities proceeded simultaneously spoke eloquently for the efficiency of the college administration, and for the excellent work of the local committee on arrangements, under the chairmanship of Henry P. Hansen.

The total registered attendance of 1095 persons was drawn from a wide geographical area. It included 67 children of unspecified ages. When these are subtracted, the net adult registration of 1028 is not far below the total of 1088 at the 1951 meeting of the division on the campus of the University of Southern California. It is an impressive attendance in view of the distance of Corvallis from the larger educational centers of California, which contributed the largest number of delegates, with Oregon a close second, and Washington next.

Although predominantly a divisional meeting, all sections of the United States were represented, and there was a gratifying attendance from western Canada. There were registrants—principally exchange professors and students in American universities—from Alaska and Hawaii and from seven foreign countries.

GEOGRAPHIC DISTRIBUTION OF REGISTRANTS*

Arizona	8	Nebraska	2
California	345	New Mexico	1
Colorado	18	New York	4
Delaware	3	**Nevada**	15
District of Columbia	2	North Dakota	4
Florida	2	Oklahoma	2
Idaho	28	**Oregon**	301
Illinois	1	South Dakota	3
Indiana	1	Texas	2
Kansas	1	**Utah**	58
Maryland	3	Virginia	1
Massachusetts	4	**Washington**	221
Mississippi	1	Wisconsin	1
Montana	9	Wyoming	6
		Total, continental United States	1047
Alaska	1	Egypt	1
Belgium	1	**Hawaii**	4
Canada		India	1
Alberta	1	Israel	1
British Columbia	31	Japan	2
China	2	Norway	3
		Total, foreign or overseas	48
		Grand total	1095

* Bold-face type indicates the six states, the territory of Hawaii, and the Canadian province comprising the Pacific Division of the AAAS. Their combined registration was 1003, or 92% of the total.

Despite final examinations and the beginning of summer schools, which prevented many teachers from attending, nearly every center of learning in the region was represented, as the following community analysis of the registrations from the three Pacific Coast states demonstrates: California, 61 communities—Davis 65, Berkeley 45, Los Angeles 27, Pasadena and Altadena 24, Palto Alto and Stanford 24, Riverside 22, Santa Barbara 14, San Francisco 10, La Jolla and Fresno 8 each; Oregon, 28 communities—Corvallis 180, Portland 50, Eugene 21. Washington, 27 communities—Seattle 62, Pullman 52, Richland 29, Prosser 14, Wenatchee 9, and Puyallup 8.

Publications Received

The Birth and Death of the Sun. George Gamow. A Lucid Explanation of Stellar Evolution and Atomic Energy. New York: New American Library of World Literature, 1952. 220 pp. Illus. 35¢.

Dictionary of Civil Defence. Carlton Wallace, Ed. London: Jordan & Sons; New York: Philosophical Library, 1952. 160 pp. Illus. $2.75.

Epilepsy, the Last of the Hush-Hush Diseases. New York: Committee for Public Understanding of Epilepsy, 1952.

Initiation a l'Embryologie Generale. Albert Dalcq. Paris: Masson, 1952. 122 pp. Illus. 920 fr.

Malaria, Chills and Fever; Ague. 8 pp. Illus. For elementary schools. ***Quinine for Relief of Night Cramps.*** 8 pp. For high school and college grades. ***Quinine and Quinidine Formulary.*** Rev. ed. 36 pp. For advanced students, college grade. ***Quinine: The Story of Cinchona.*** Norman Taylor. 15 pp. Illus. History, geography, and public health classes. ***The Technique of Blood Examination in Malaria.*** 24 pp. Illus. For advanced students of college grade. P. O. Box 368, Radio City Station, New York: Cinchona Products Institute, 1952. Free.

Microbial Growth and its Inhibition. Monograph Ser., No. 10. First International Symposium on Chemical Microbiology. Mixed language edition containing articles in either English or French, with summaries in both languages. Geneva: WHO, 1952. iv + 286 pp. Illus. 15/–; $3.00; Fr. fr. 960; Sw. fr. 12.

Mount McKinley and the Alaska Range in Literature. A Descriptive Bibliography. Bradford Washburn. Boston: Museum of Science, 1951. 88 pp.

Nutrition in the Practice of Medicine, with Comments on Nutrition, Disease and Geography. Proc. Nutrition Symposium held at the University of California, School of Medicine, San Francisco, October 30, 1951. J. Arnold Bargen *et al.* New York: National Vitamin Foundation, 1952. 163 pp. Illus. $1.50.

Recent Developments and Techniques in the Maintenance of Standards. Proceedings of a Symposium held at the National Physical Laboratory on 21st and 22nd May 1951. London, H. M. Stat. Off., 1952. 100 pp. Illus. 4s. 6d.

Soda Fountain and Luncheonette Equipment. Standard No. 1, National Sanitation Foundation Standards. Ann Arbor, Mich.: National Sanitation Foundation, 1952. 58 pp. Illus. 50¢.

Substances Naturelles de Synthèse. Vol. IV, ***Préparations et Méthodes de Laboratoire.*** Léon Velluz, Ed. Paris: Masson, 1952. 165 pp. Illus. 1800 fr.

Toward a Regional Program of Forestry. Rept. Commission on Forestry and Related Training. Atlanta, Ga.: Southern Regional Education Board, 1952. 55 pp.

***Viruses as Causative Agents in Cancer. Ann. N. Y. Acad. Sci.*, 54,** Art. 6. C. P. Rhoads *et al.* New York: N. Y. Acad. Sci., 1952. 400 pp. Illus. $4.00.

Weighing Vehicles in Motion. Pub. 211. Highway Research Board, Bull. 50. Washington: National Academy of Sciences—National Research Council, 1952. 27 pp.

Meetings & Conferences

Oct. 18. Ways of Science Conference (Annual). Roosevelt College, Chicago.

Oct. 18–24. National Metal Congress and Exposition, sponsored by the American Society for Metals, American Welding Society, American Institute of Mining and Metallurgical Engineers, and Society for Non-Destructive Testing. Philadelphia.

Oct. 19–21. Industrial Recreation Conference (Annual). Purdue University, Lafayette, Ind.

Oct. 19–23. National Rehabilitation Association (Annual). Seelbach Hotel, Louisville, Ky.

Oct. 20–21. Independent Petroleum Association of America (Annual). Mayo Hotel, Tulsa.

Oct. 20–22. American Oil Chemists' Society (Fall). Netherland-Plaza Hotel, Cincinnati.

Oct. 20–22. Detroit Institute of Cancer Research (Annual). Engineering Society of Detroit, Mich.

Oct. 20–24. American Ornithologists' Union (Annual). Baton Rouge.

Oct. 20–24. American Public Health Association (Annual). Public Auditorium, Cleveland.

Oct. 20–24. American Society for Metals. Convention Hall, Philadelphia.

Oct. 20–24. National Safety Council. Conrad Hilton Hotel. Chicago.

Oct. 21–24. American Dietetic Association. Auditorium, Minneapolis.

Oct. 23–24. Independent Petroleum Association of America (Annual). The Skirvin, Oklahoma City.

Oct. 23–24. Tanners Council of America (Fall). Edgewater Beach Hotel, Chicago.

Oct. 24–25. Western Institute on Epilepsy (Annual). Los Angeles.

Oct. 25. American Mathematical Society (Eastern). Yale University, New Haven, Conn.

Oct. 25–30. National Society for Crippled Children and Adults. Fairmont Hotel, San Francisco.

Oct. 27. American Gas Association (Annual). Auditorium, Atlantic City.

Oct. 27–28. Society of Exploration Geophysicists. Conference on Mining Exploration. King Edward Hotel, Toronto.

Oct. 27–29. National Lubricating Grease Institute (Annual). Edgewater Beach Hotel, Chicago.

Oct. 27–30. Electrochemical Society. Montreal.

Oct. 28. Association of Consulting Chemists and Chemical Engineers, Inc. (Annual Symposium). Hotel Belmont Plaza, New York.

Oct. 29–31. American Chemical Society, Division of Rubber Chemistry (Fall). Hotel Statler, Buffalo, N. Y.

Oct. 29–31. Canadian Entomological Society. Quebec.

Oct. 29–Nov. 1. Audio Engineering Society (Annual). Hotel New Yorker, New York.

Oct. 30–31. Society of Exploration Geophysicists, Pacific Coast Section. Hotel Statler, Los Angeles.

Oct. 30–Nov. 1. National Association for Music Therapy (Annual). Hotel Kansan, Topeka.

Nov. 2–5. Southern Psychiatric Association. The Greenbriar, White Sulphur Springs, W. Va.

Nov. 2–8. Inter-American Congress of Radiology. Mexico City.

Nov. 6–7. Pittsburgh Diffraction Conference (Annual). Mellon Institute, Pittsburgh.

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RESEARCH GRANTS

1953 ARCTIC RESEARCH GRANTS

The Arctic Institute of North America is offering a number of research grants in 1953 for scientific investigations dealing with arctic and subarctic regions. Research must include field investigations in North America or studies at one of the Institute offices. Completed applications must be received by 1st December 1952. Application forms may be obtained from: Arctic Institute of North America, 1530 P Street, N.W., Washington 5, D. C., or 3485 University Street, Montreal 2, Canada.

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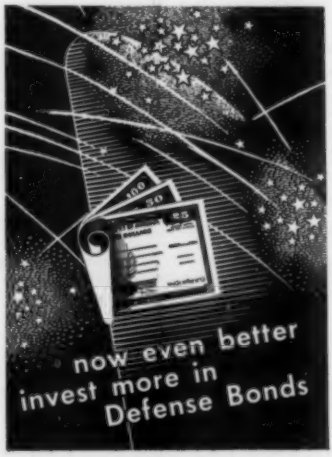

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119th AAAS MEETING

St. Louis, Mo., December 26-31, 1952

The list of hotels and their rates and the reservation coupon below are for your convenience in making your hotel room reservation in St. Louis. Please send your application, *not* to any hotel directly, but to the AAAS Housing Bureau in St. Louis and thereby avoid delay and confusion. The experienced Housing Bureau will make assignments promptly; a confirmation will be sent you in two weeks or less. **Share a room with a colleague if you wish to keep down expenses.** Mail your application *now* to secure your first choice of desired accommodations. All requests for reservations must give a definite date and estimated hour of arrival, as well as date and approximate hour of departure.

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LENNOX D	5.00– 7.00	6.50– 9.00	8.50– 9.50	13.00 & up
MAJESTIC D	3.25– 4.50	5.25– 6.25	7.00– 8.00	10.00–15.00
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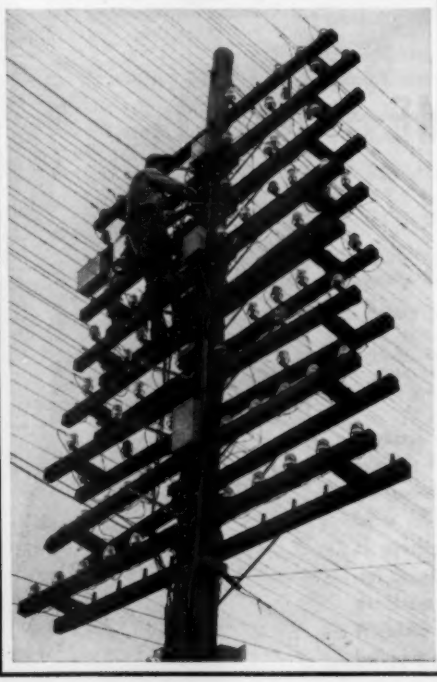

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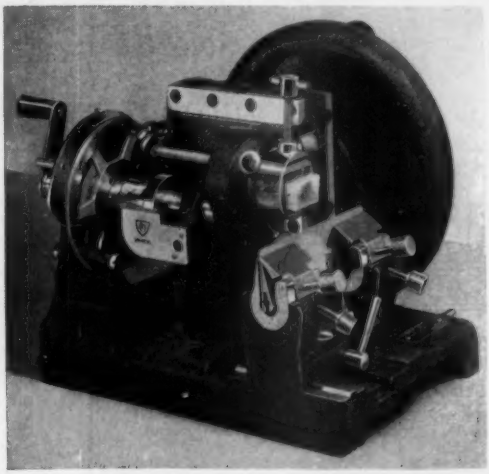
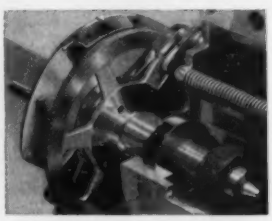
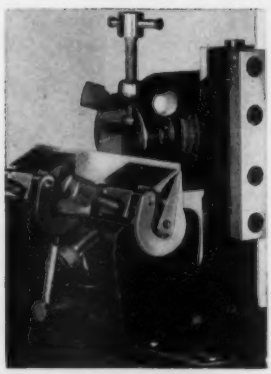


Uniform Serial Sectioning with the AO NO. 815 ROTARY MICROTOME



Sturdy, independent feed screw can be set for specimens 2 to 40 microns thick.



Improved double width knife clamps provide rigid support and wide range of tilt.

For a medium size microtome with all the accuracy and mechanical advantages for which AO Spencer Microtomes have long been famous — choose the popular No. 815 Rotary Microtome. Uniform serial sections may be cut from two to forty microns in thickness. Total excursion of the feed is 22mm. Improved ball and flange object clamp holds the block rigidly and may be oriented in any desired plane. A precision-edged, highest quality steel knife is supplied complete with back and handle for sharpening. Ask your AO distributor to show you the No. 815 Microtome, or write Dept. K2.

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